

2331/112

May 27, 2003

U.S. Application No. 09,821,850



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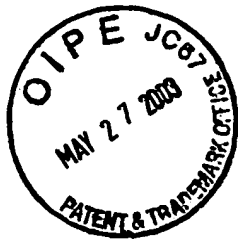
Substitute Formal Drawings

for

U.S. Application No. 09/821,850

**"Systems and Methods for Characterizing a Biological Condition or
Agent Using Selected Gene Expression Profiles"**

Bevilacqua et al.



#09592601

6692916

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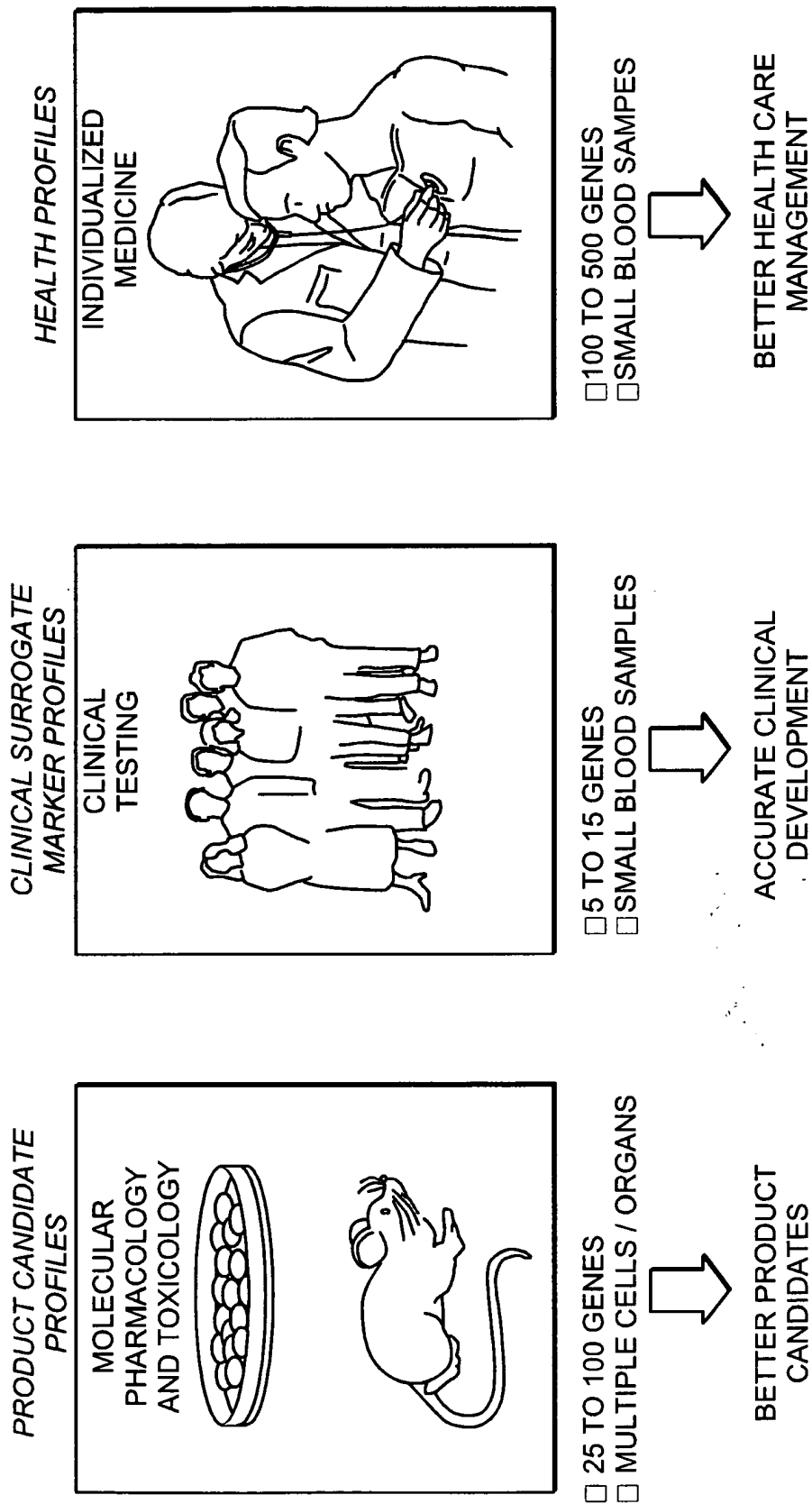
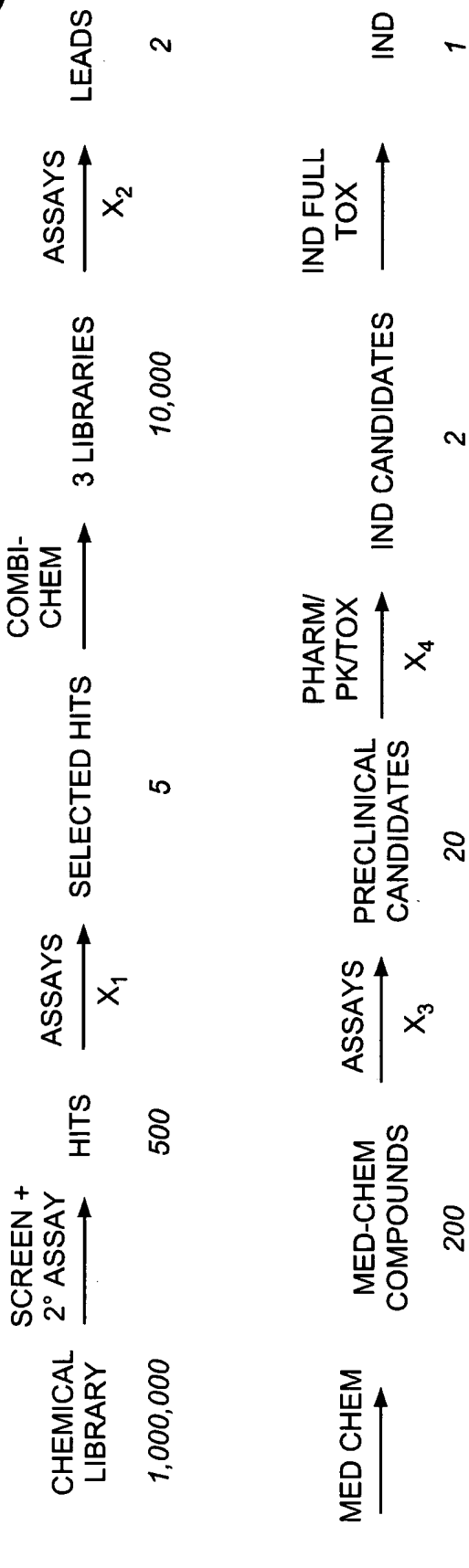
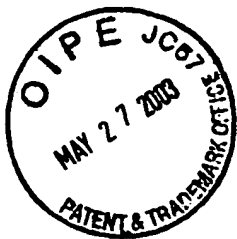


FIG. 1

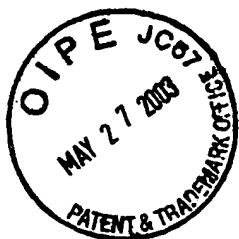


$X_1, X_2, X_3 =$ PHYSIOCHEMICAL ANALYSIS
IN VITRO TOXICOLOGY
GENE EXPRESSION PROFILING

$X_4 =$ IN VIVO GENE PROFILING

$X_5 =$ SURROGATE MARKER

FIG. 2



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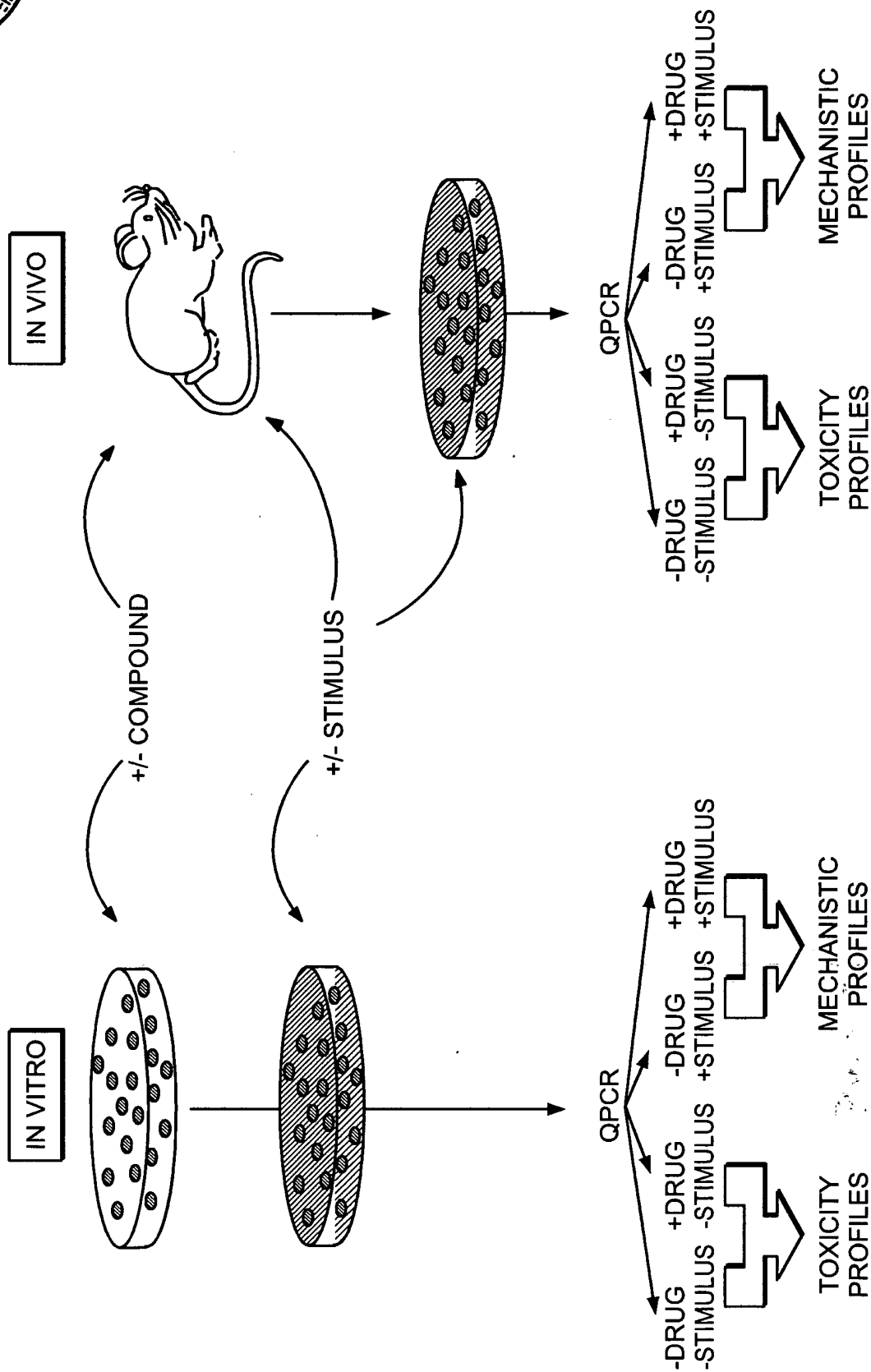


FIG. 3



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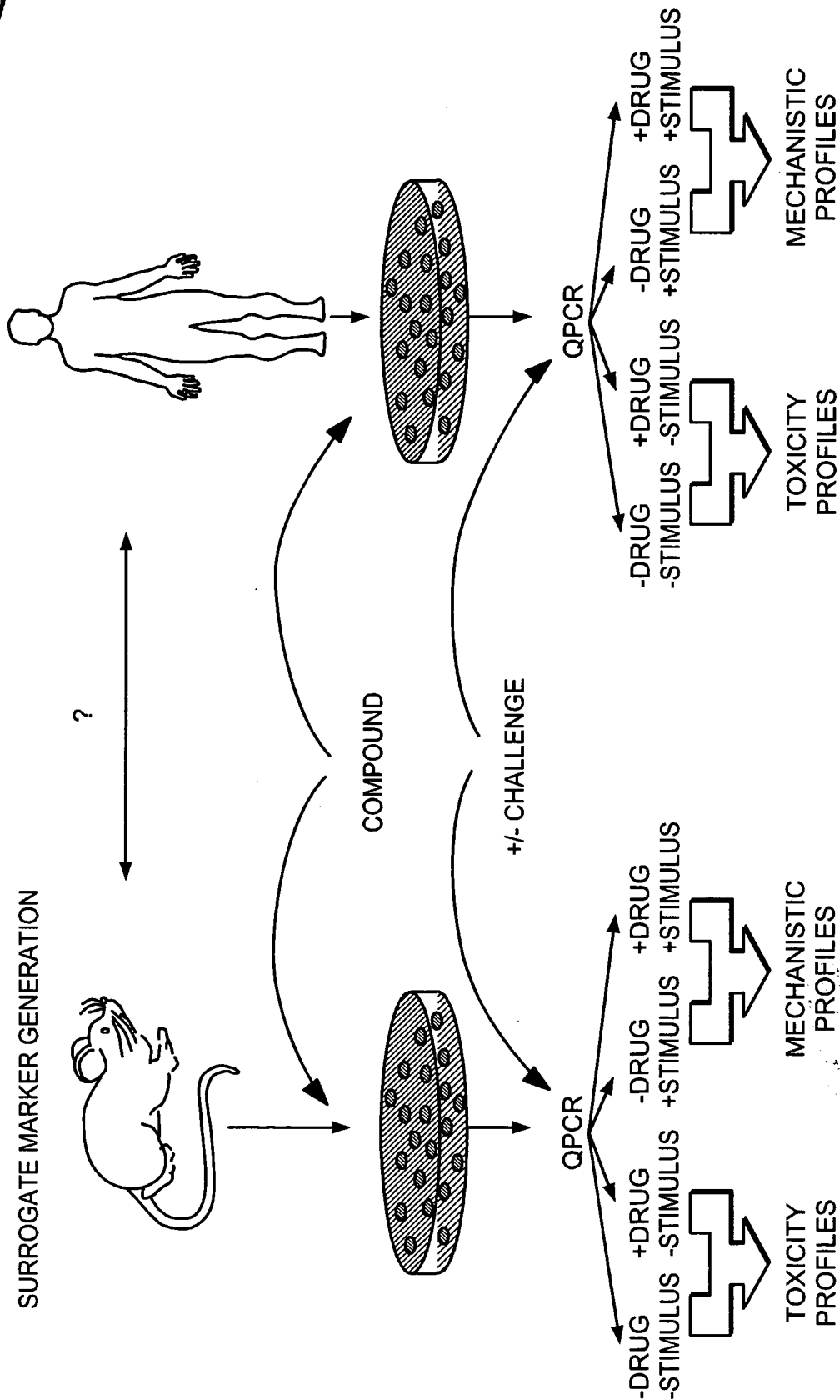


FIG. 4



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PRODUCING A "CALIBRATED SELECTED PROFILE"

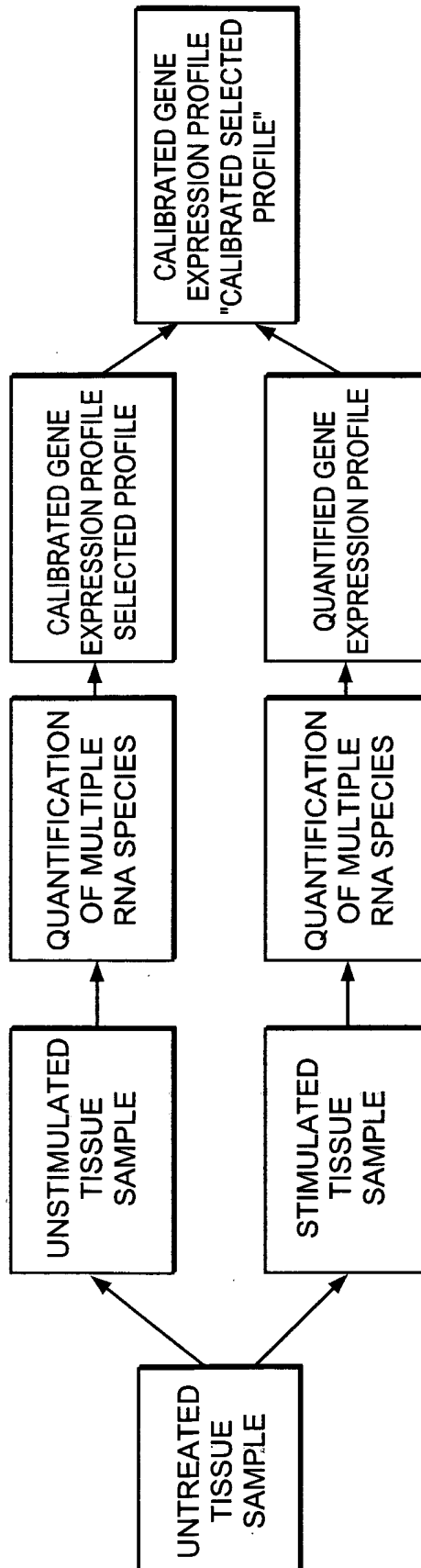


FIG. 5

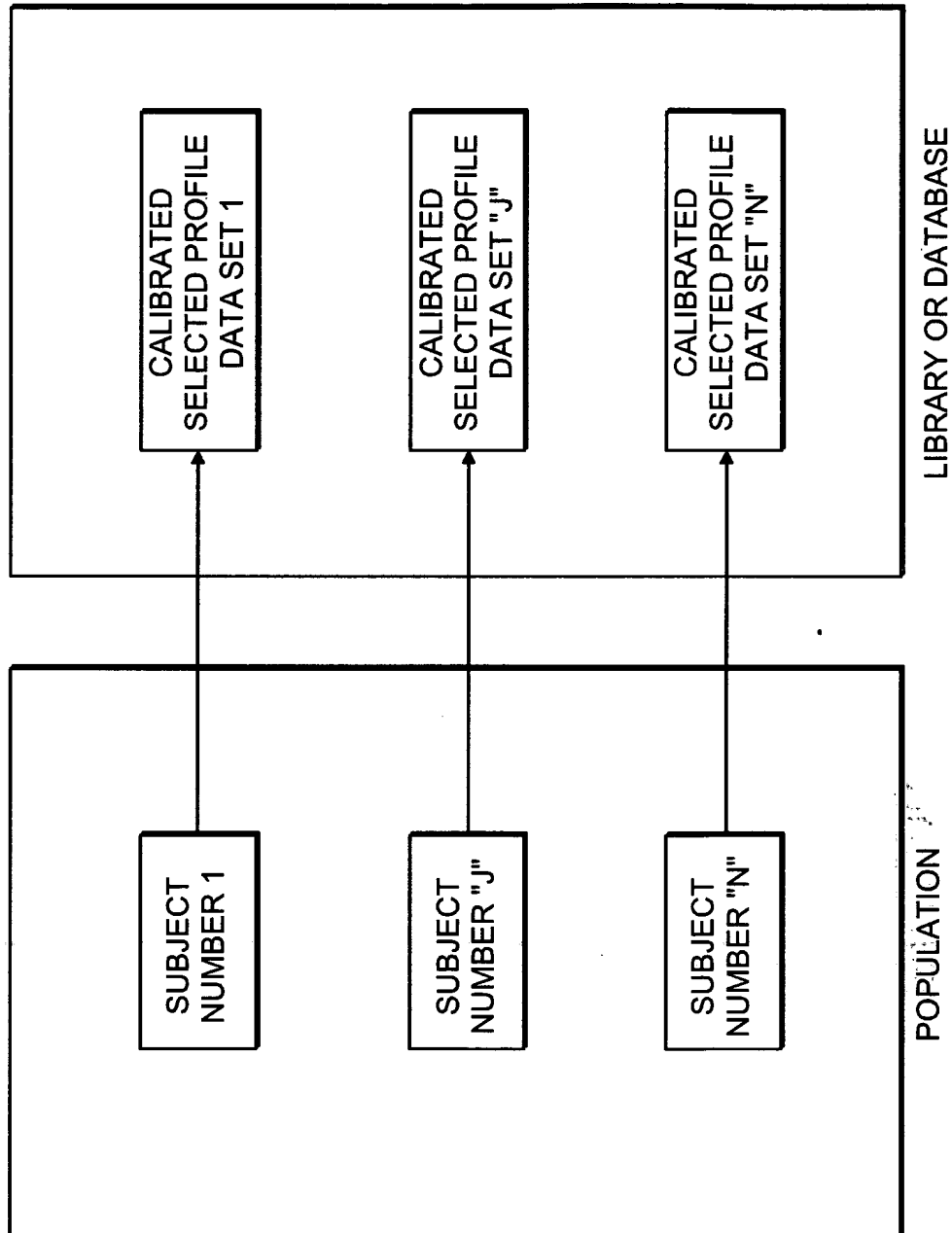
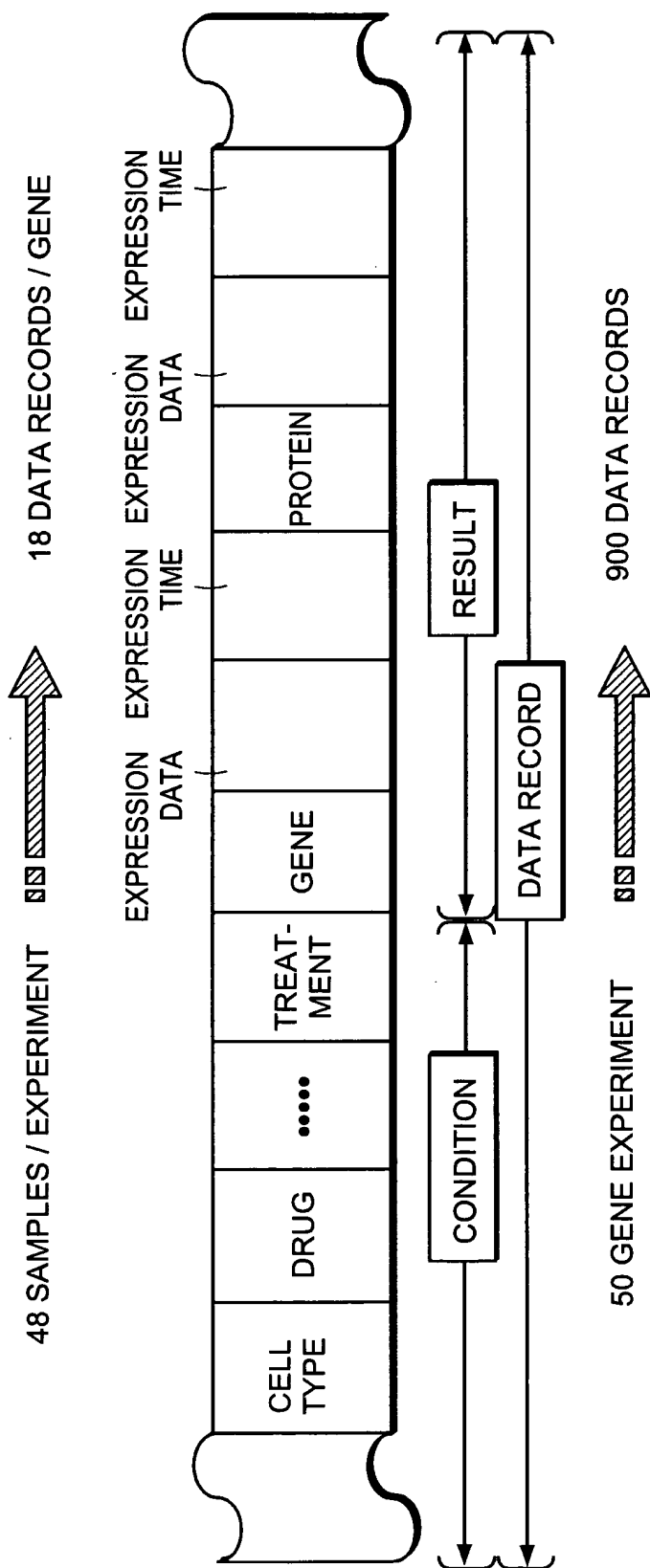
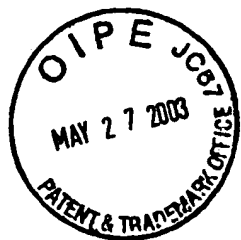


FIG. 6

100-031 27 MAY 2003



EACH NEW RECORD IMPROVES THE PREDICTIVE POWER OF THE DATABASE AND INCREASES ITS VALUE

FIG. 7



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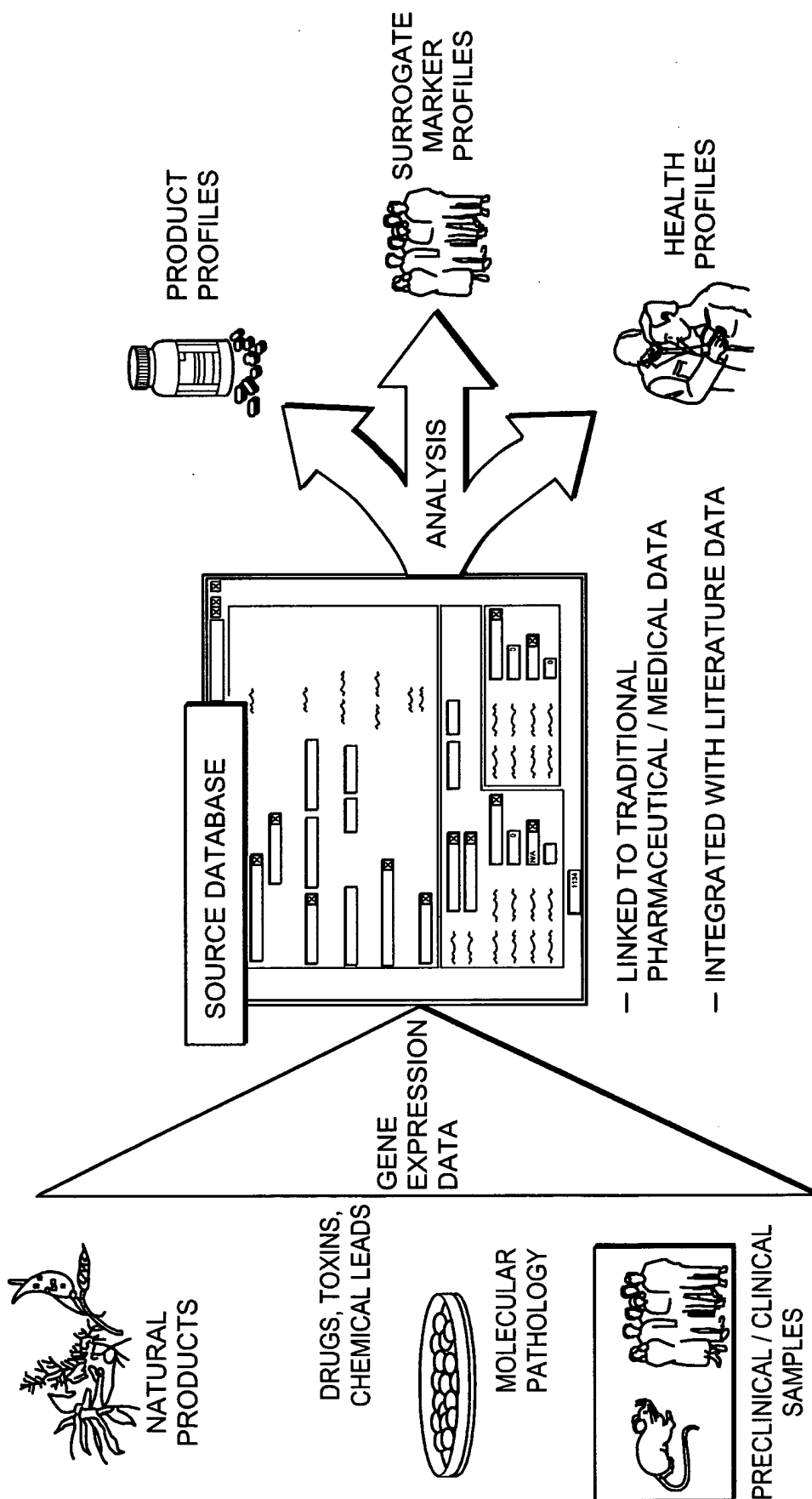


FIG. 8



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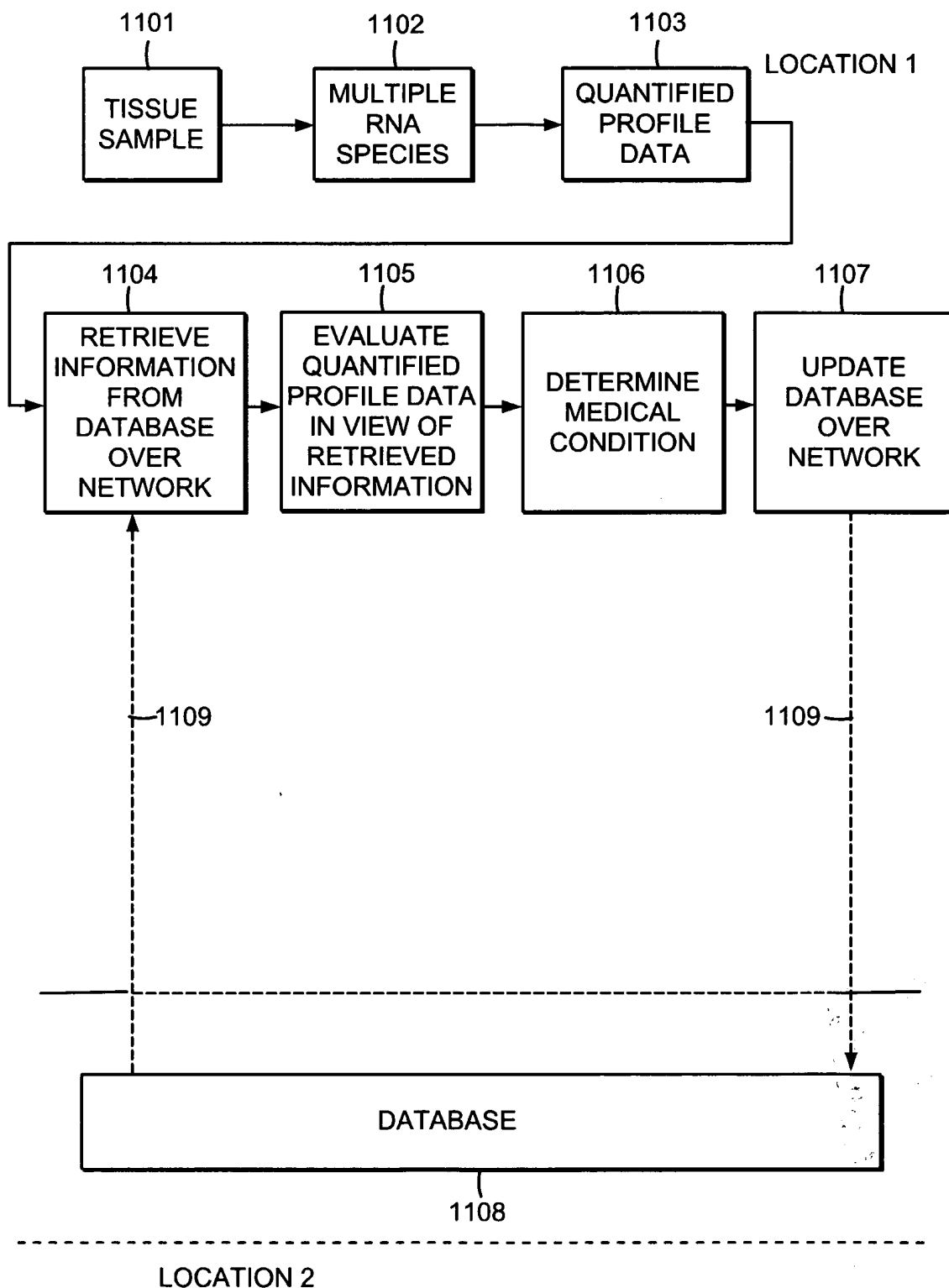


FIG. 9



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PHASE TWO CLINICAL TRIAL DESIGN USING SELECTED PROFILING

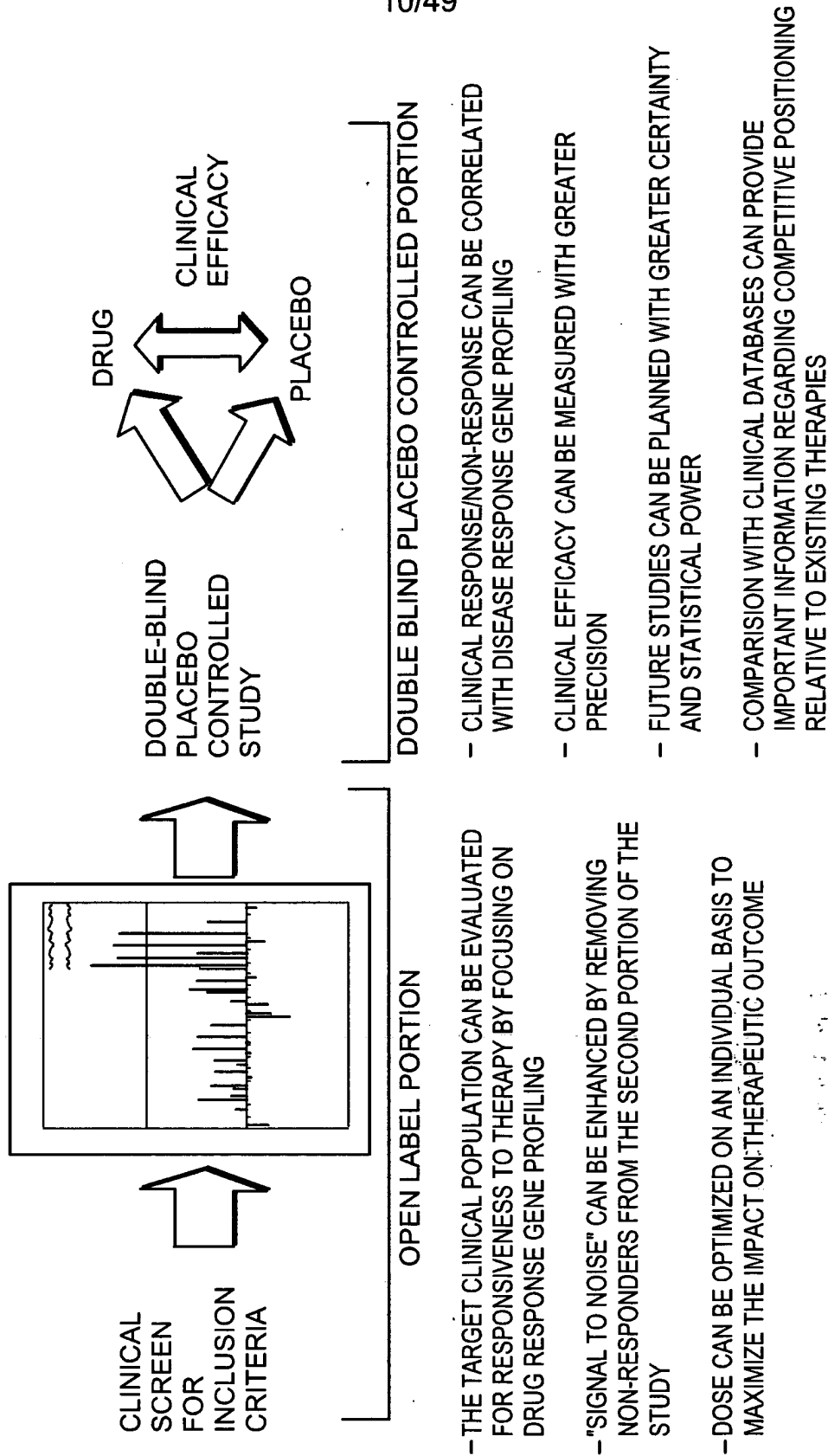


FIG. 10a

FIG. 10b

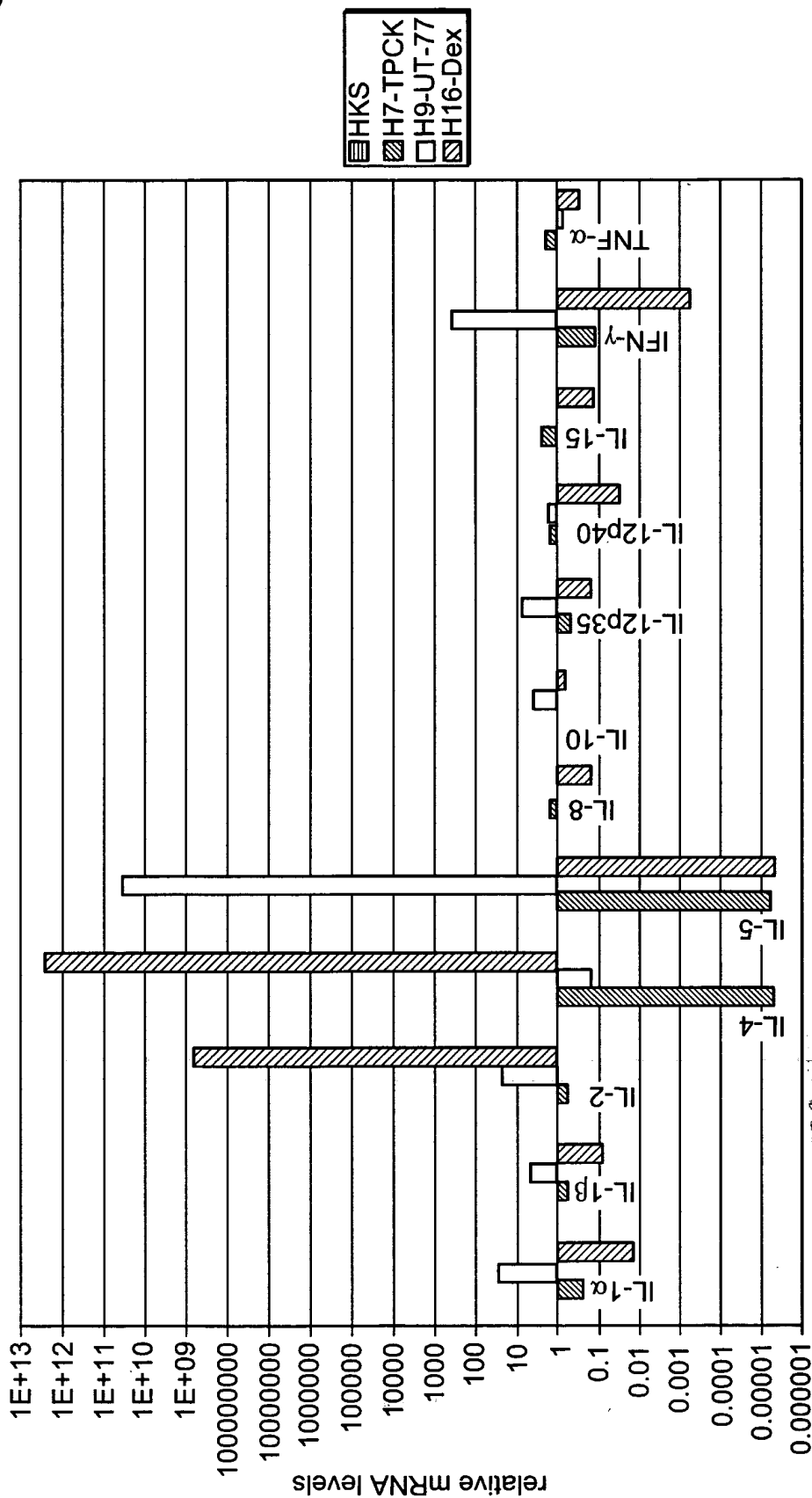


FIG. 11a



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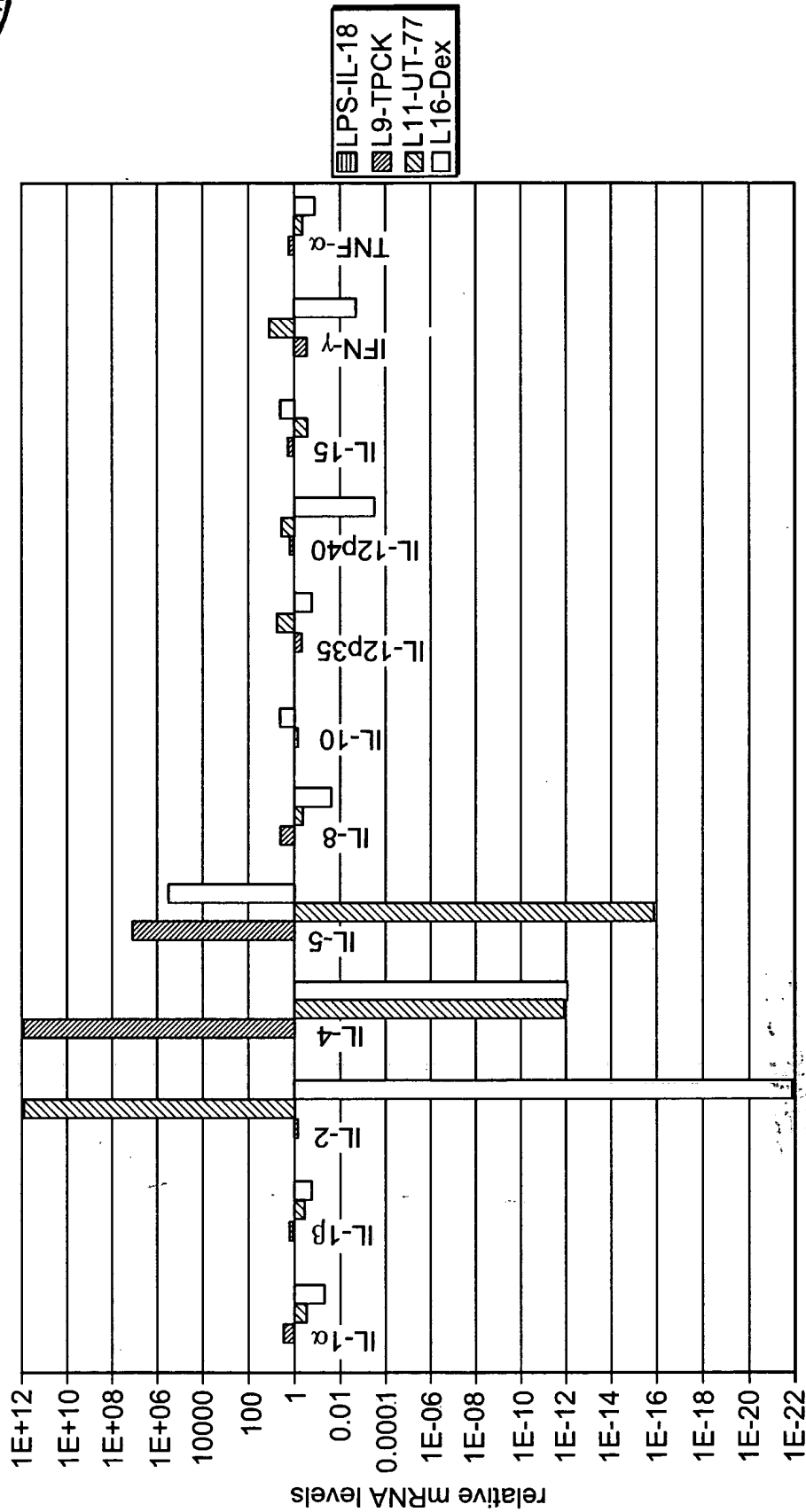


FIG. 11b



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COMPARATIVE DRUG PROFILING SHOWS DIFFERENCES AMONG ANTI-INFLAMMATORY DRUGS WITH DIFFERENT MECHANISM OF ACTION

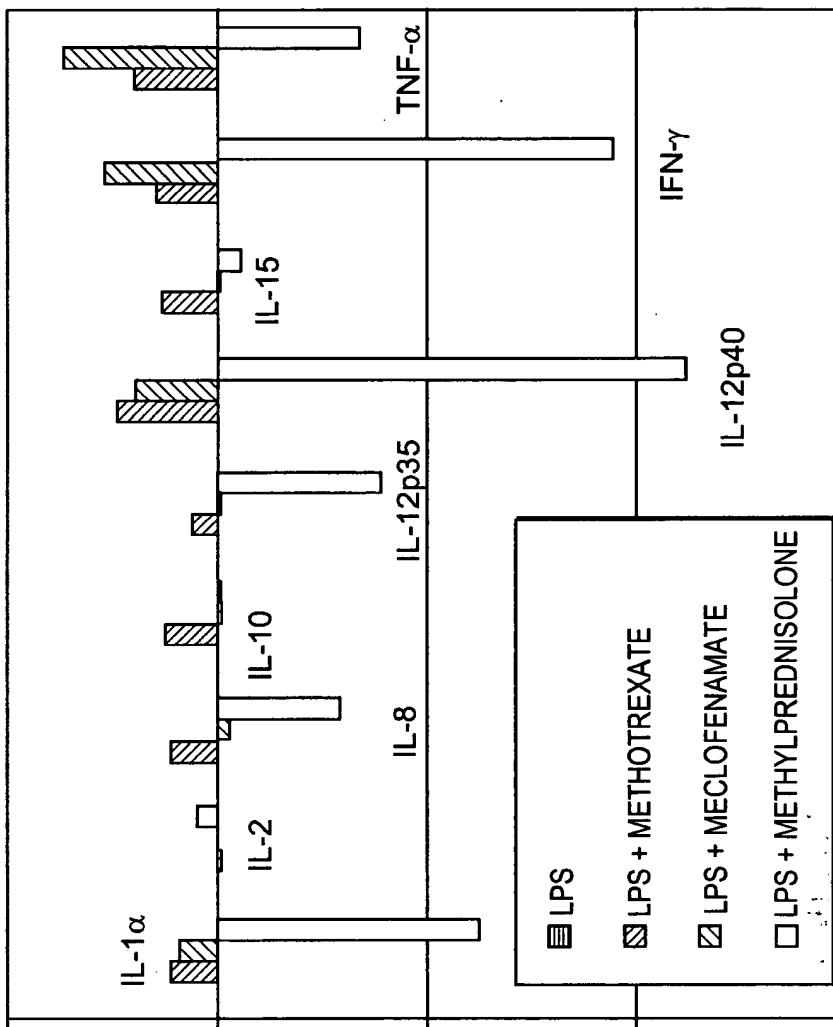


FIG. 12a



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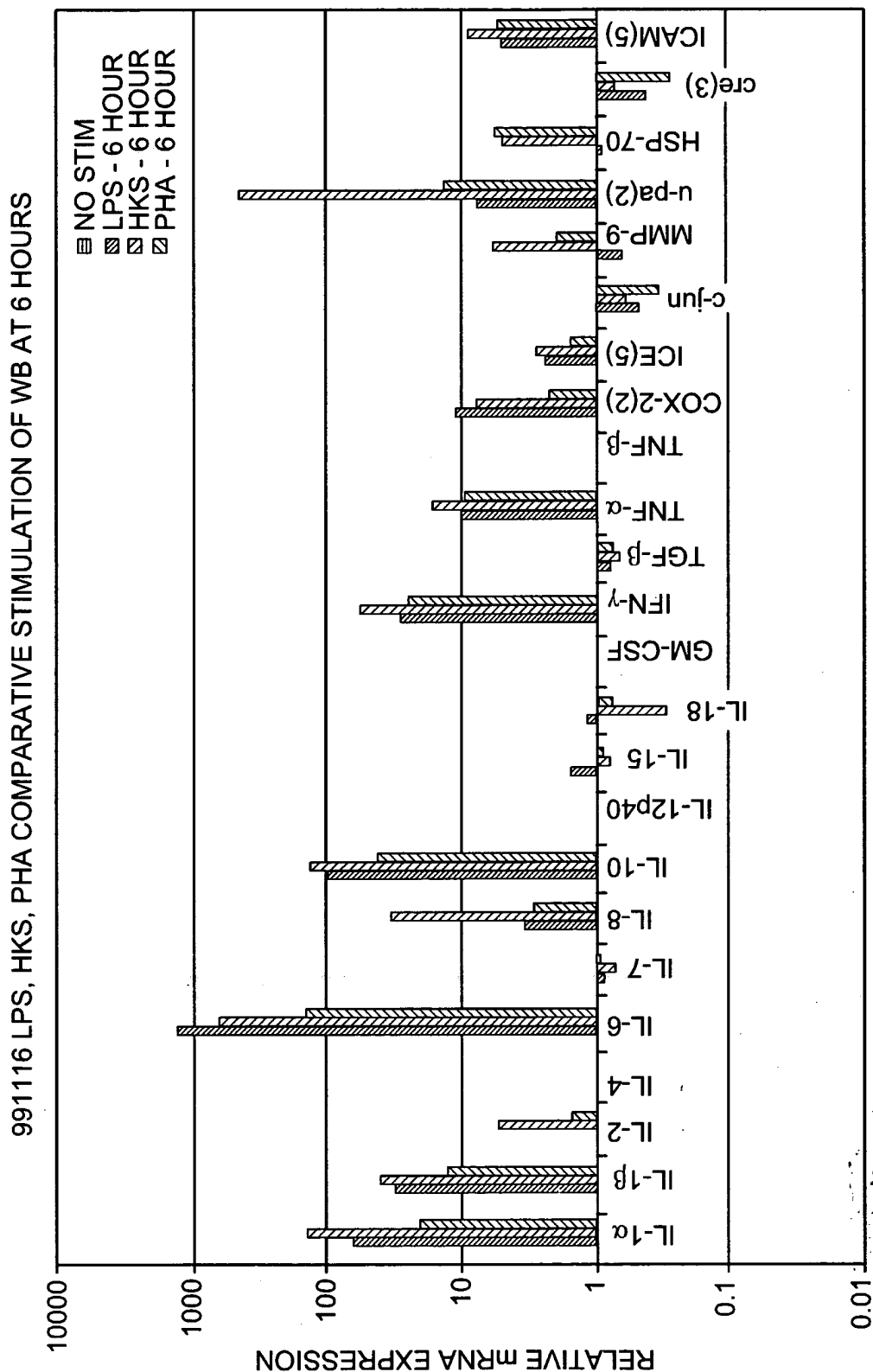


FIG. 13a

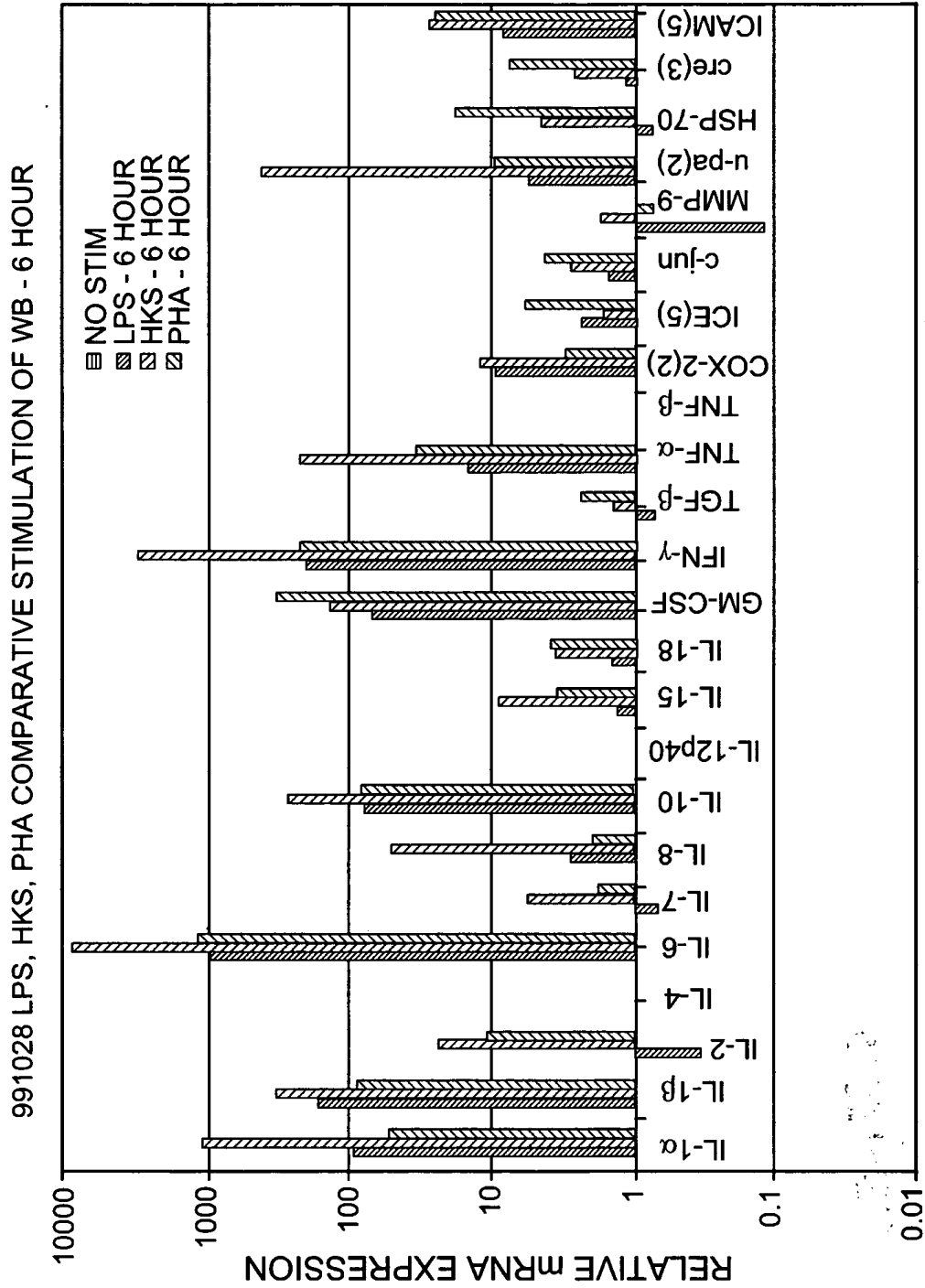


FIG. 13b



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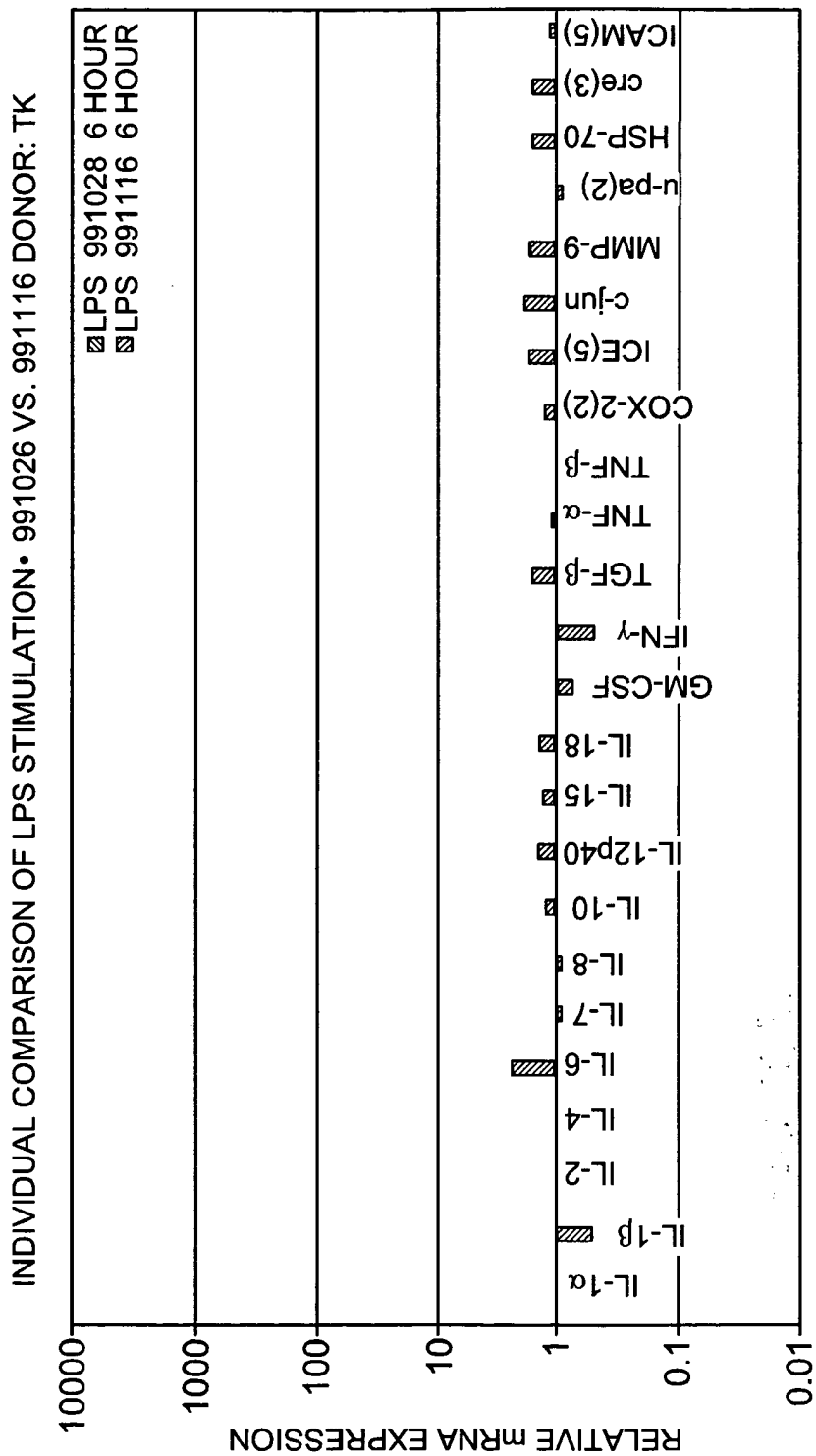


FIG. 13c



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INDIVIDUAL COMPARISON OF DONOR SAMPLE WITH NO STIMULATION
6 HOUR - 991028 VS. 991116 DONOR: TK

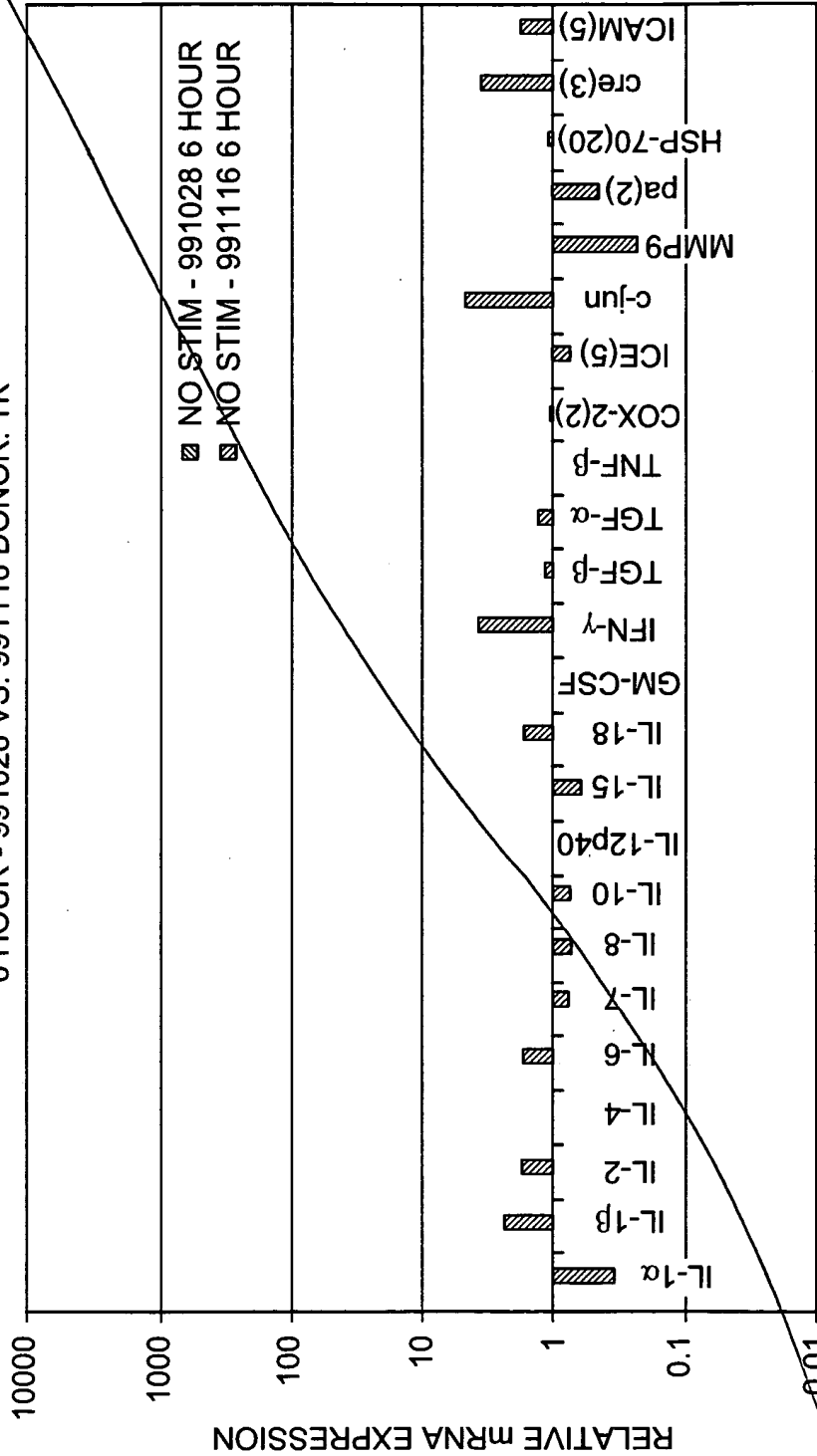


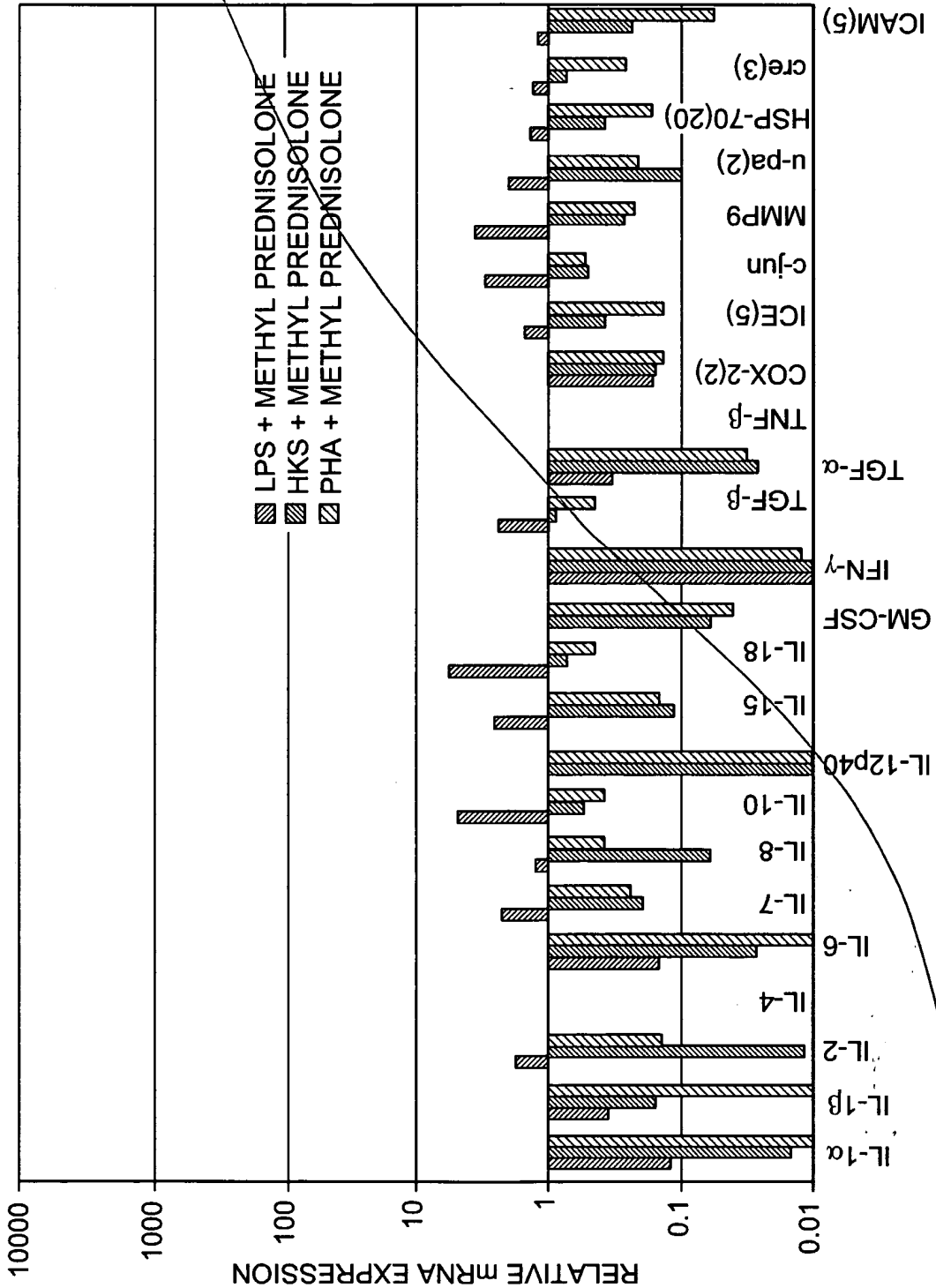
FIG. 13d



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FIG. 14

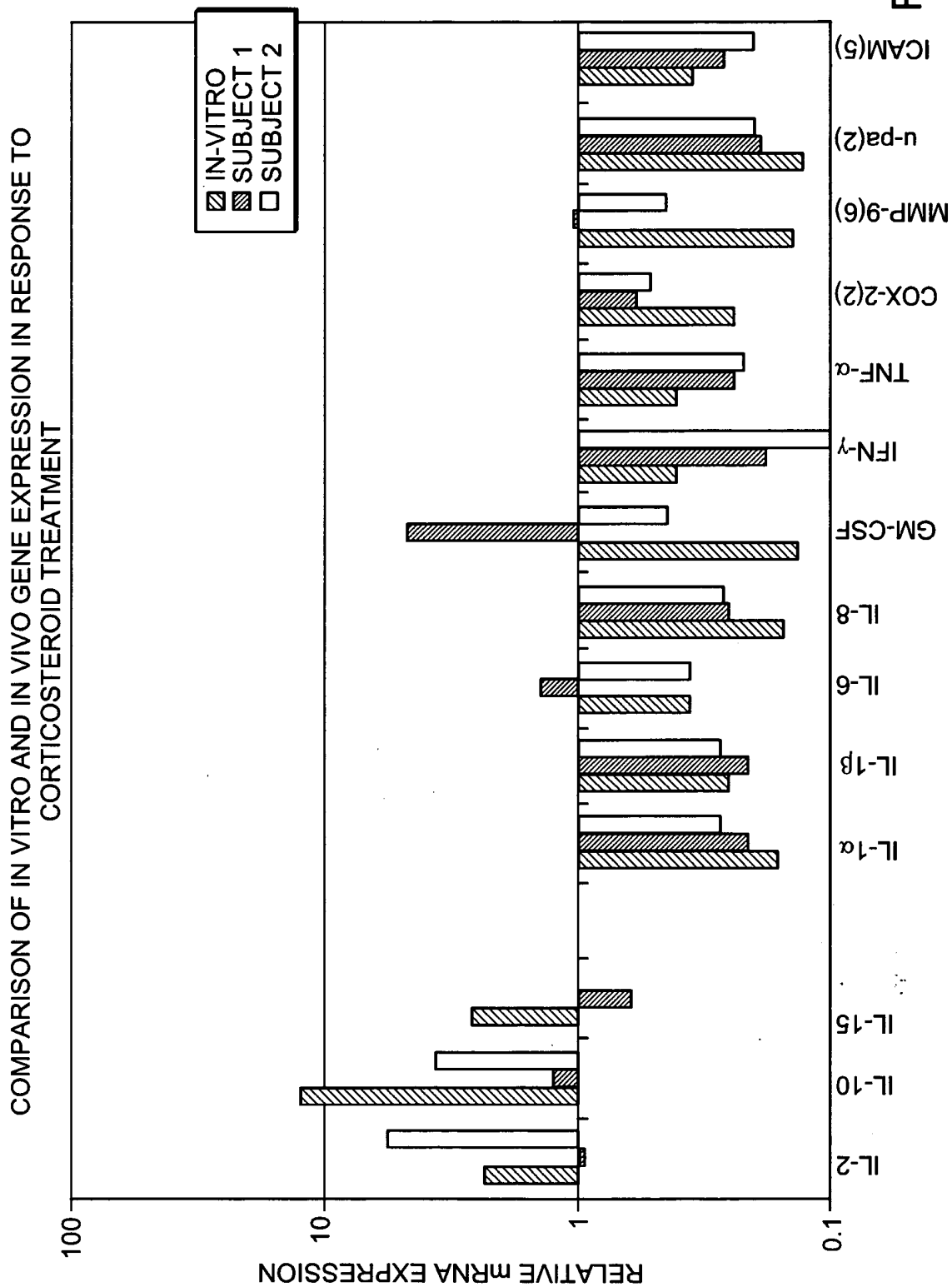
STIMULANT EFFECT ON METHYL PREDNISOLONE GENE EXPRESSION IN WHOLE BLOOD - 6 HOUR





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FIG. 15





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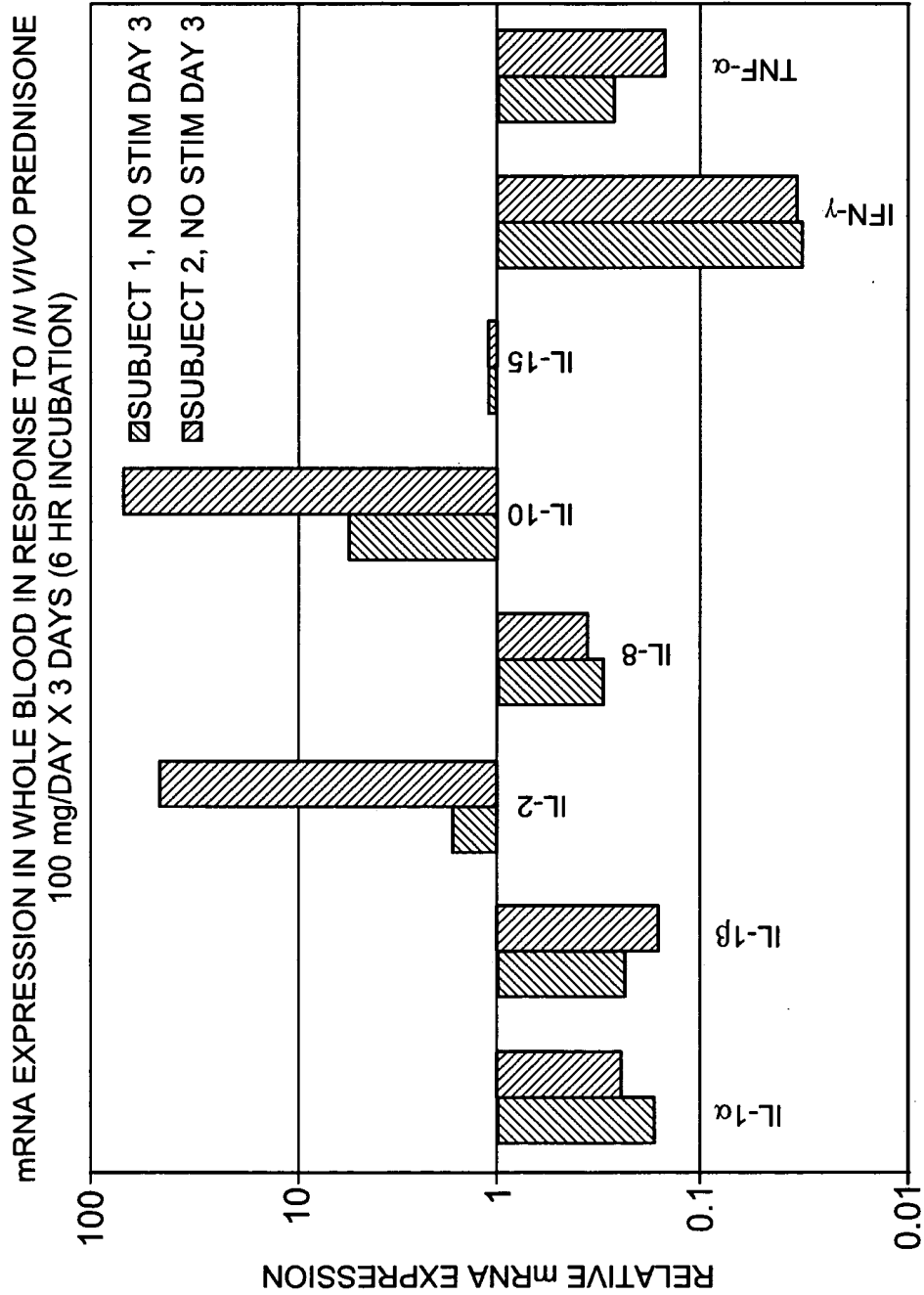


FIG. 16a



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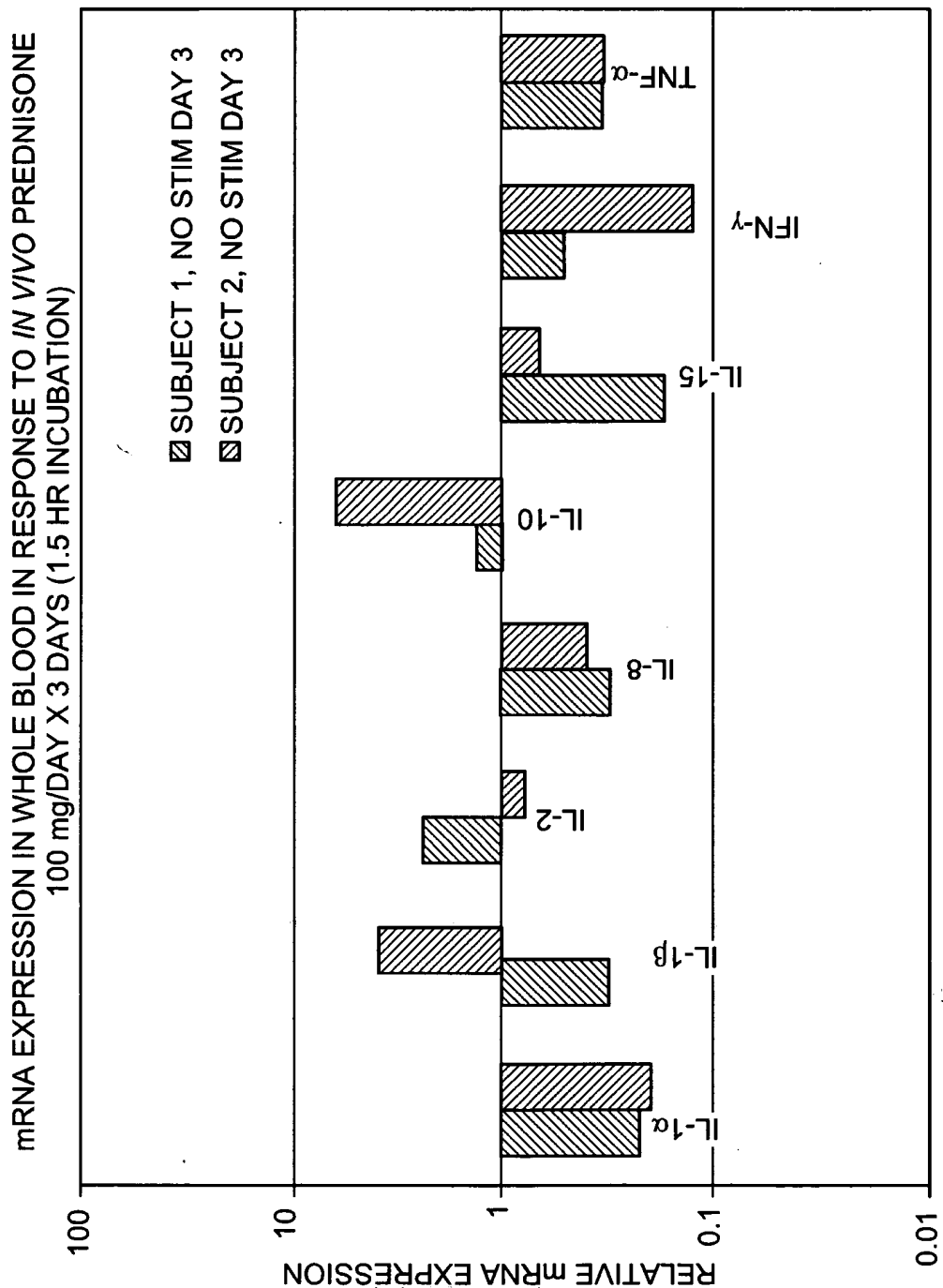


FIG. 16b



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INDIVIDUAL COMPARISON - 991028 VS. 991116
DONOR: TK

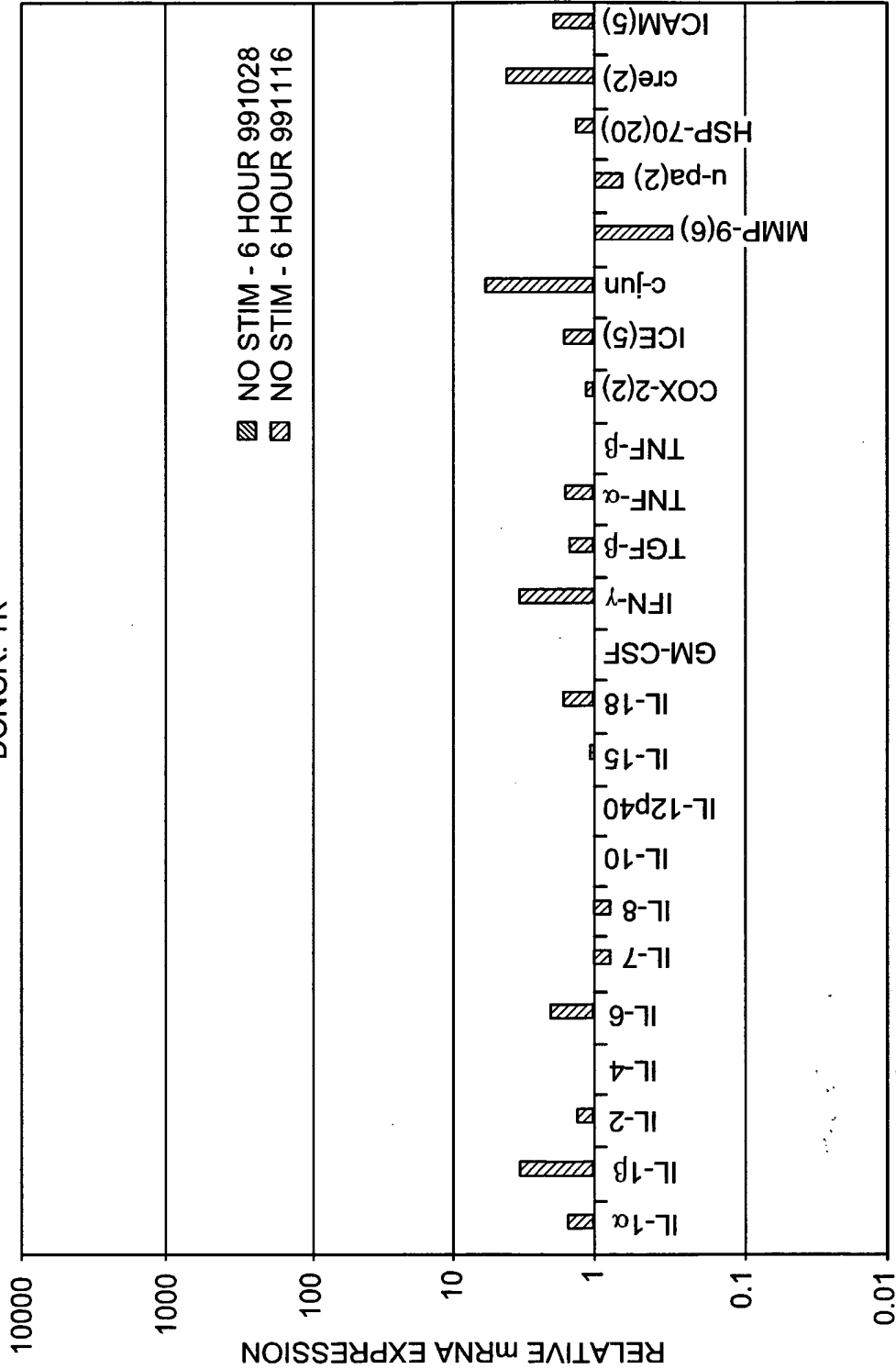


FIG. 17



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PB001 STUDY 2, STAGE 3
EFFECTS OF DRUG ON WHOLE BLOOD
DONOR 1

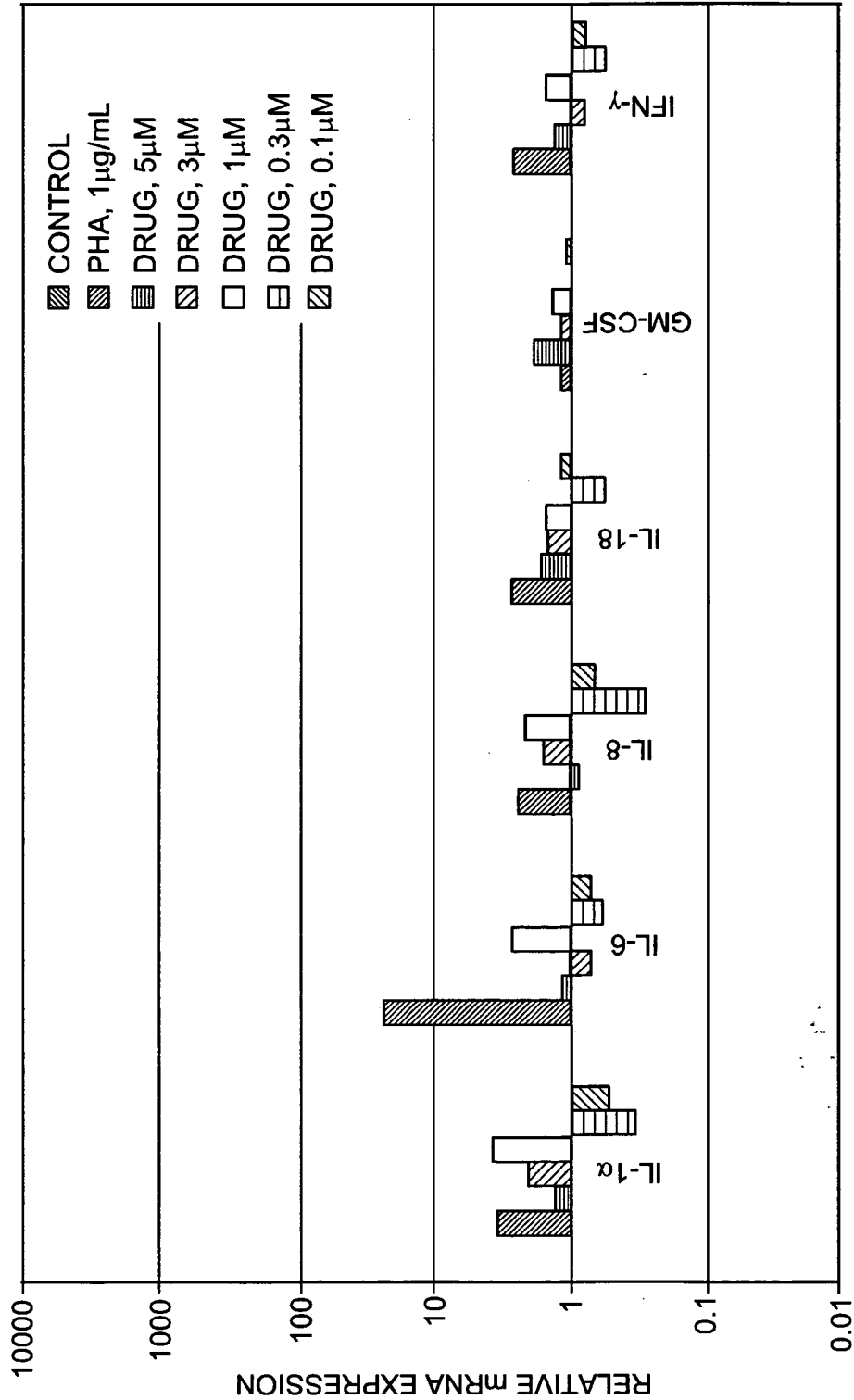


FIG. 18a



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PB001 STUDY 2, STAGE 3
EFFECTS OF DRUG ON WHOLE BLOOD
DONOR 2

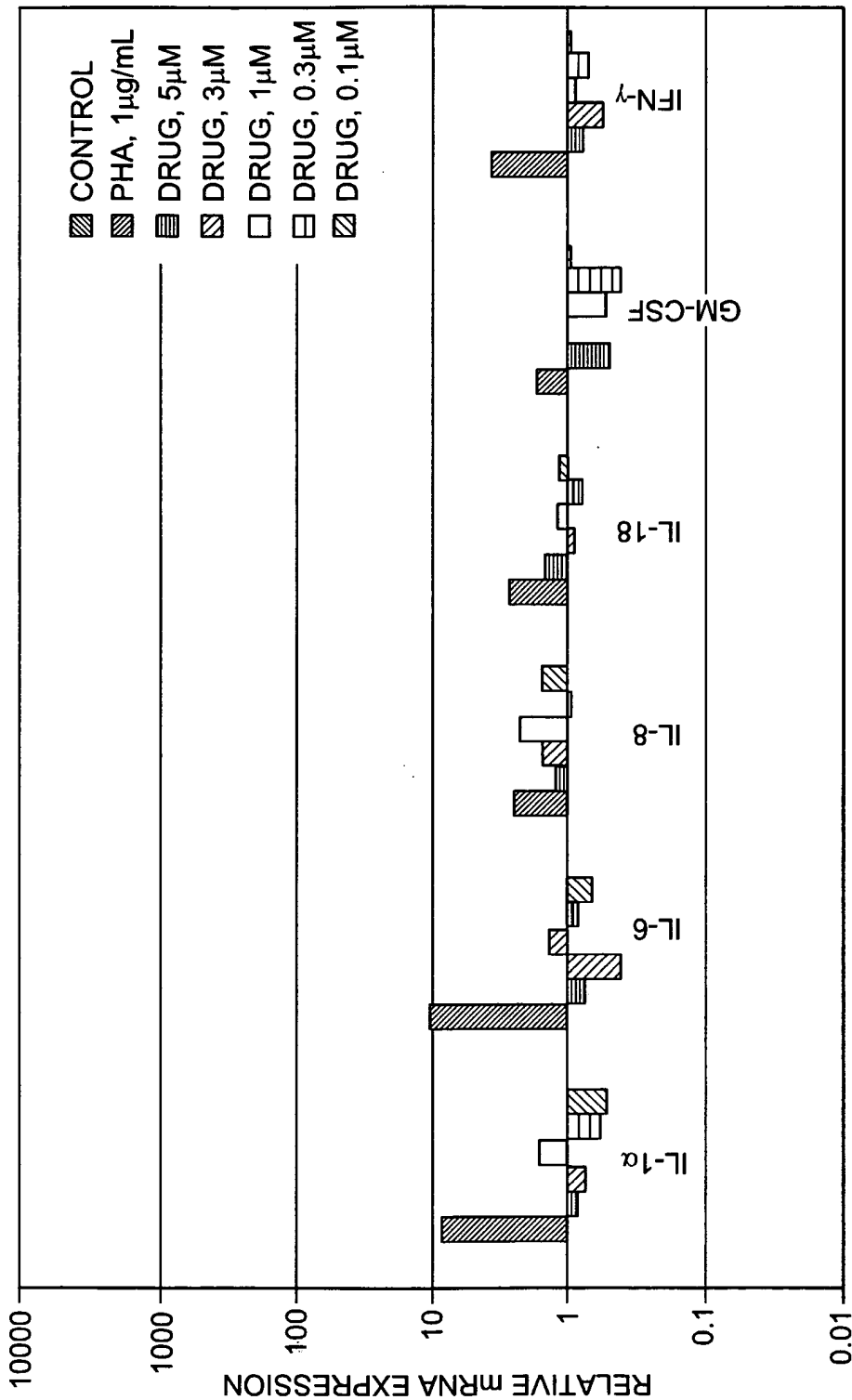
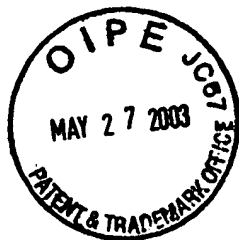


FIG. 18b



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PB001 STUDY 2, STAGE 3
EFFECTS OF DRUG ON WHOLE BLOOD
DONOR 3

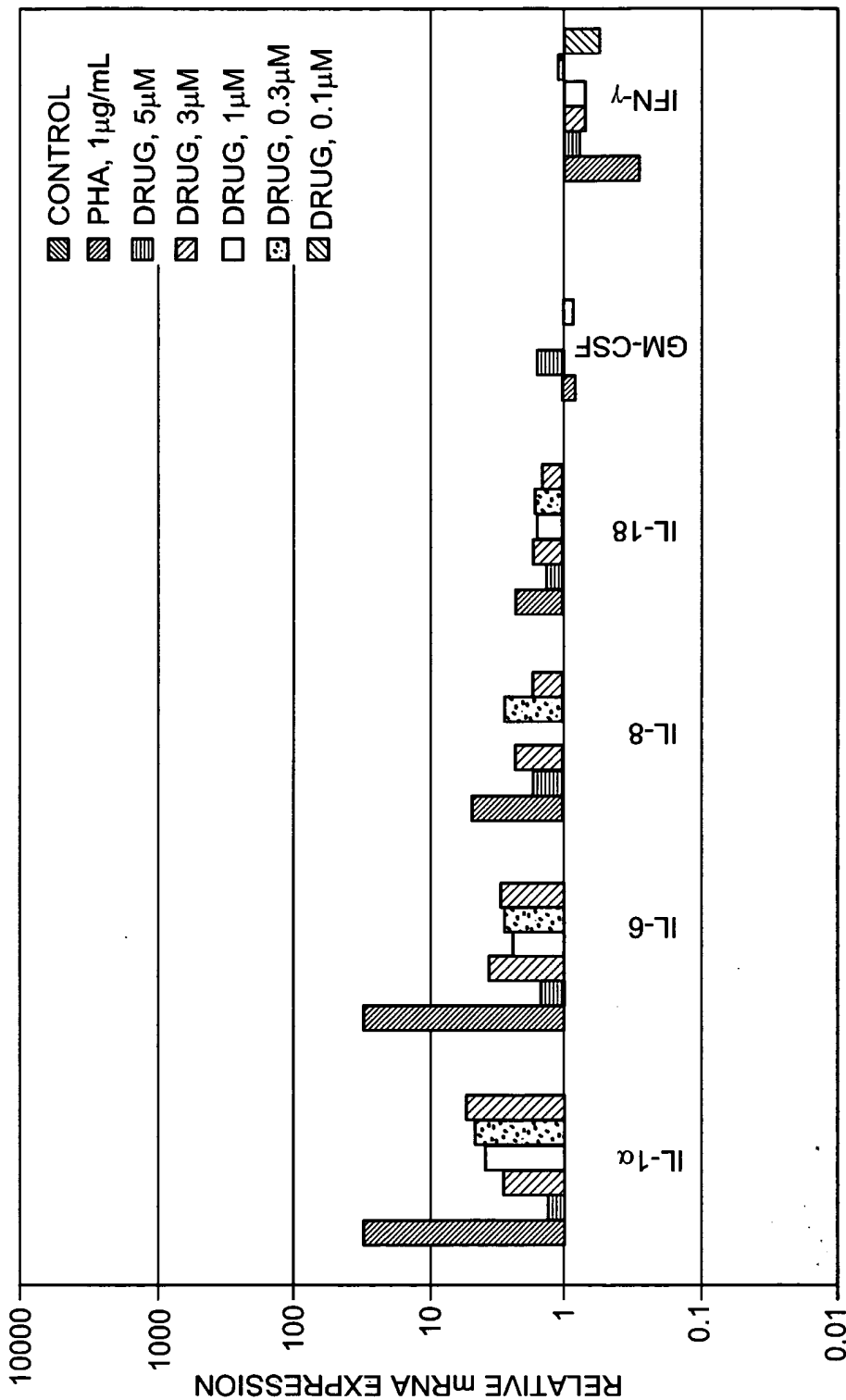


FIG. 18c



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PB001 STUDY 2, STAGE 3
EFFECTS OF DRUG ON WHOLE BLOOD
DONOR 4

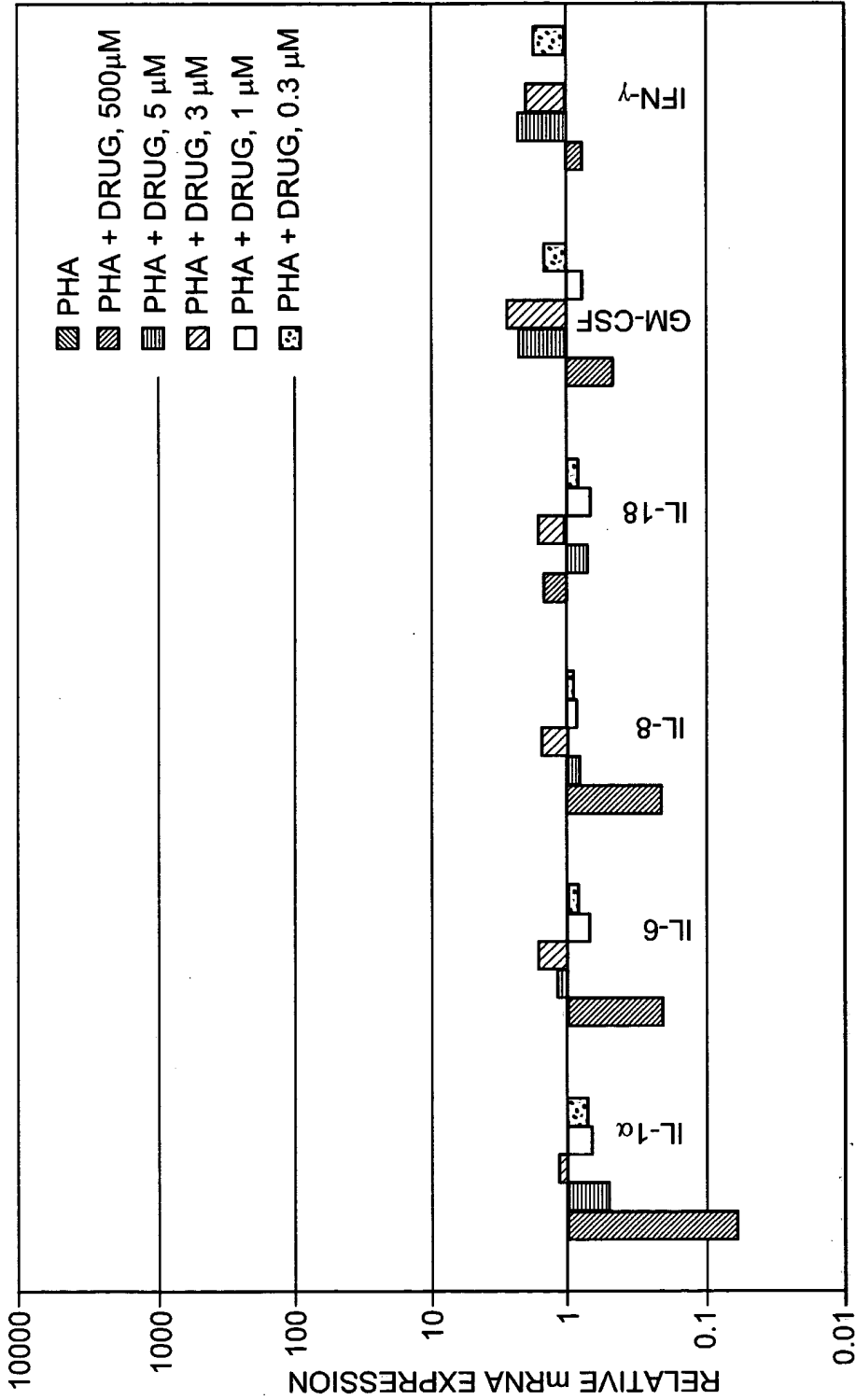


FIG. 18d



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PB001 STUDY 2, STAGE 3
EFFECTS OF DRUG ON WHOLE BLOOD
DONOR 5

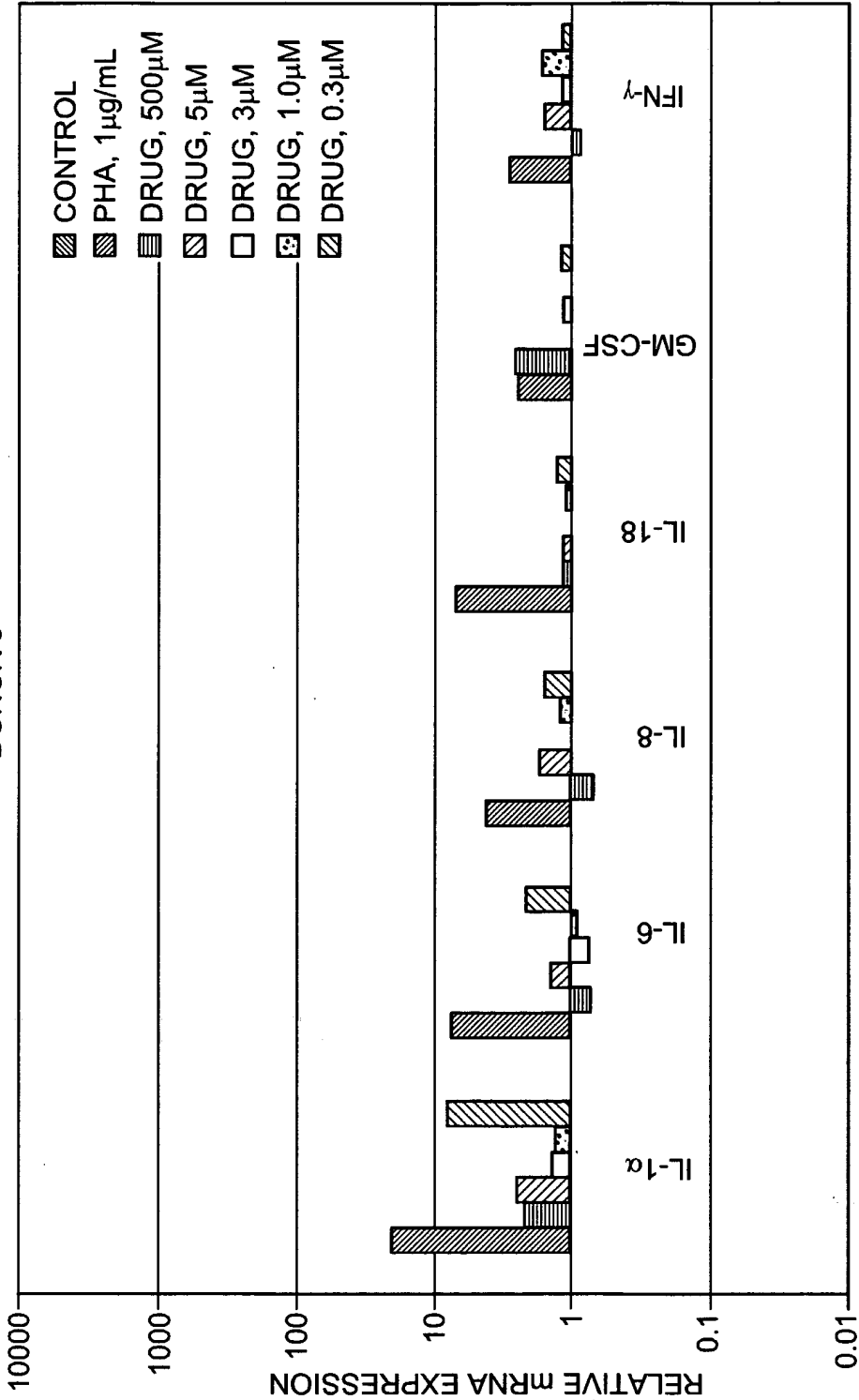


FIG. 18e



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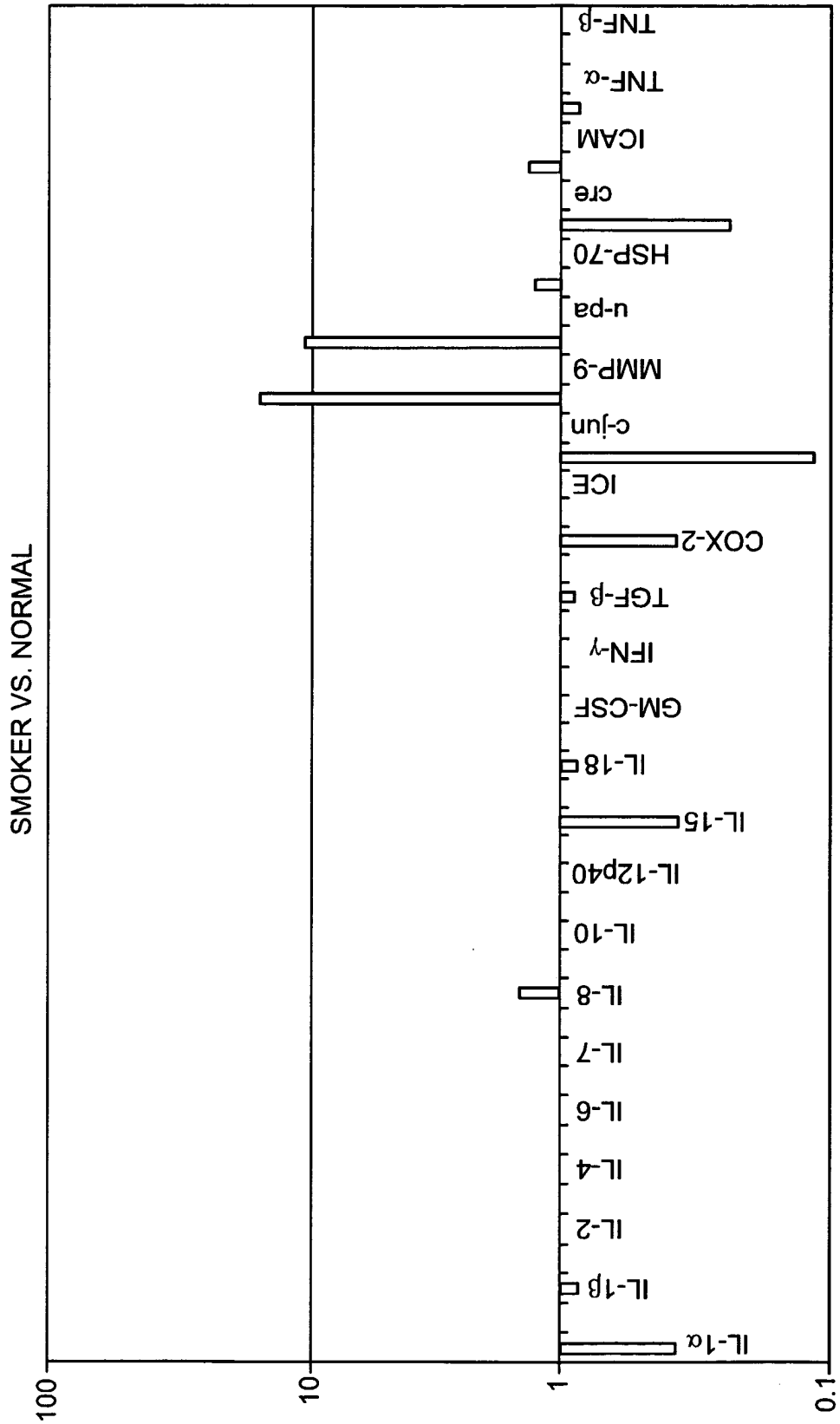


FIG. 19a



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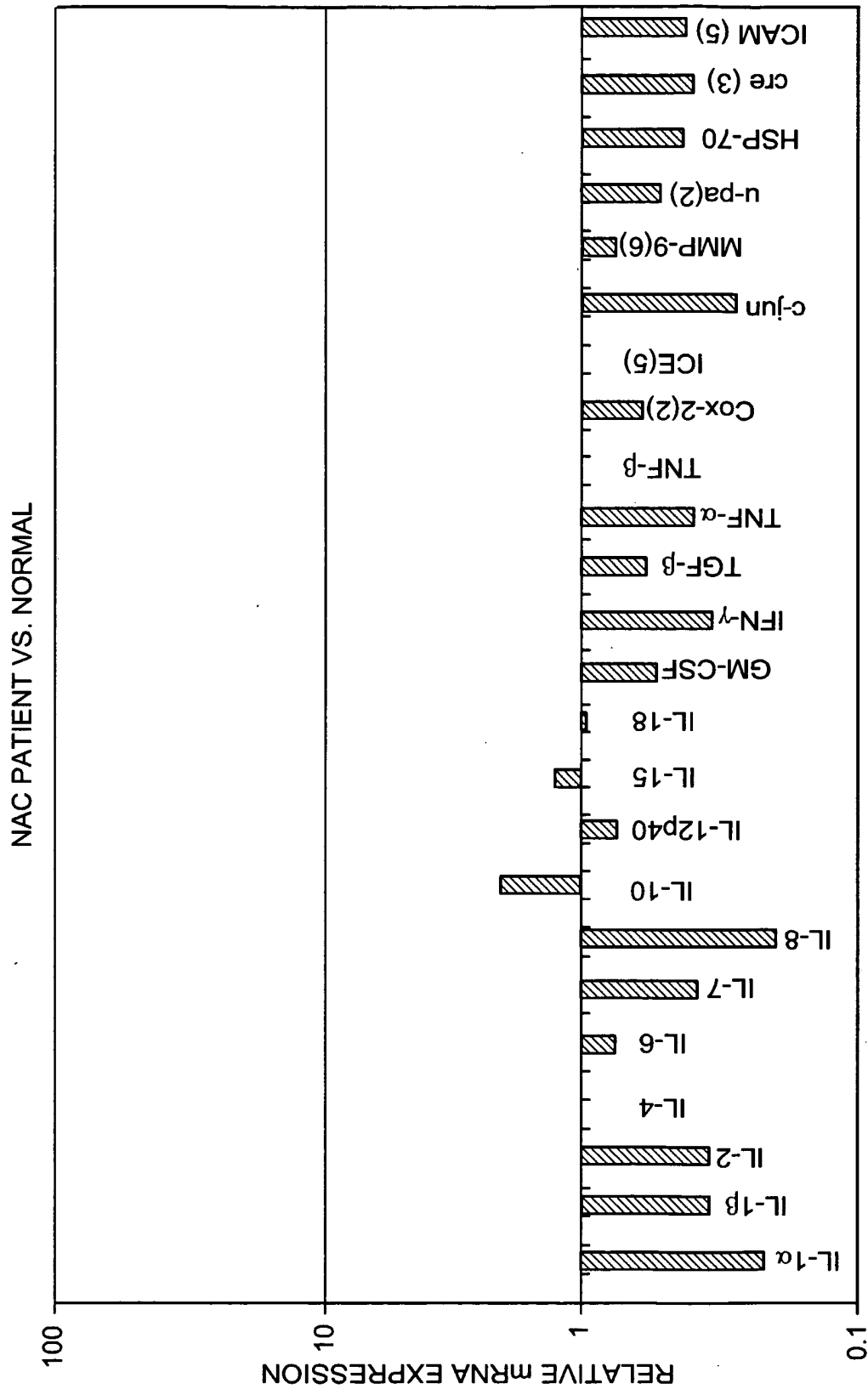


FIG. 19b



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EXPRESSION OF GST-P GENE IN INDIVIDUAL RATS FOLLOWING A TOXIC DOSE OF ACETAMINOPHEN

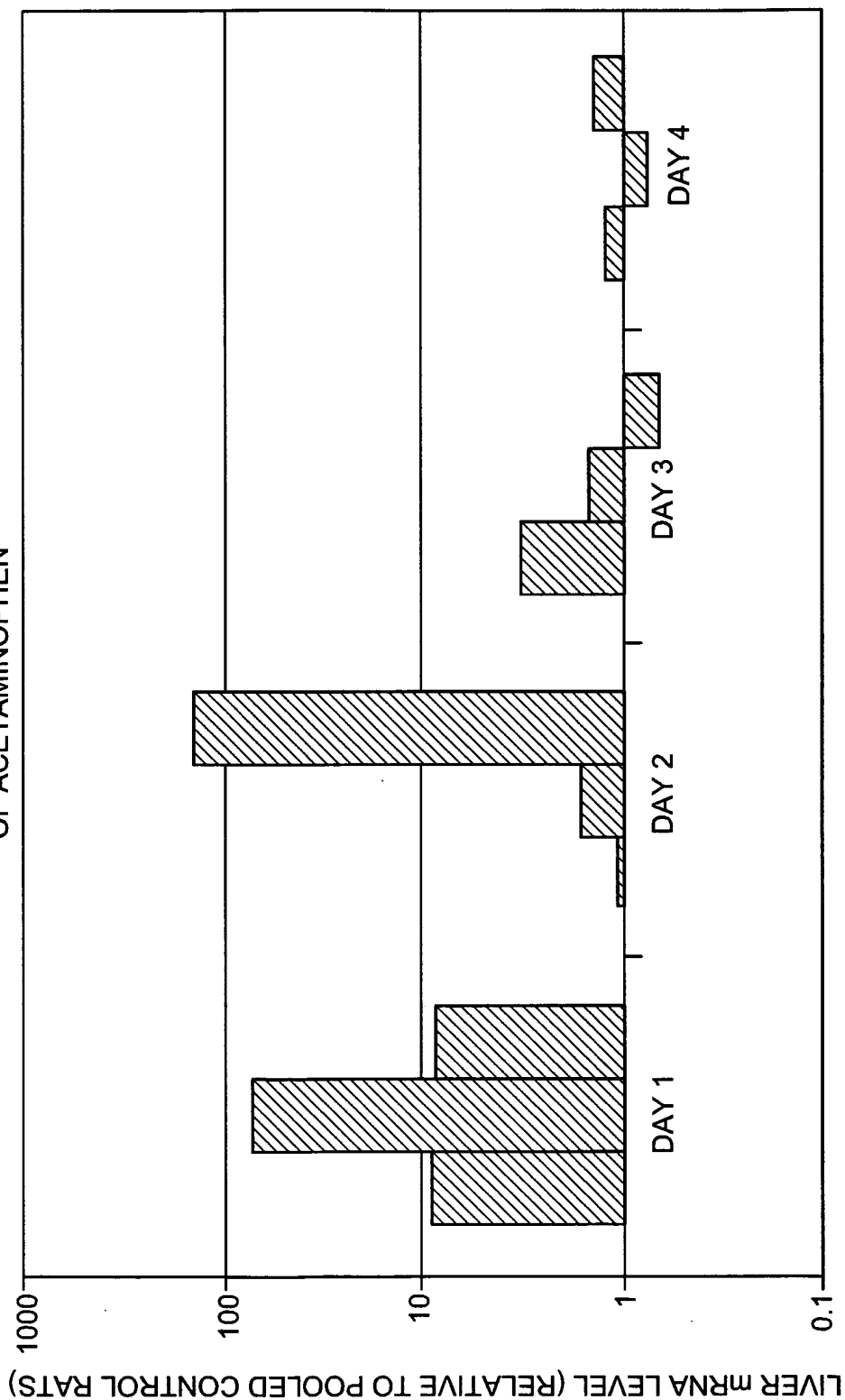


FIG. 20



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COMPARATIVE HERBAL PROFILING SHOWS DIFFERENCES AMONG ANTI-INFLAMMATORY HERBS SUCH AS ECHINACEA, ARNICA AND SIBERIAN GINSENG

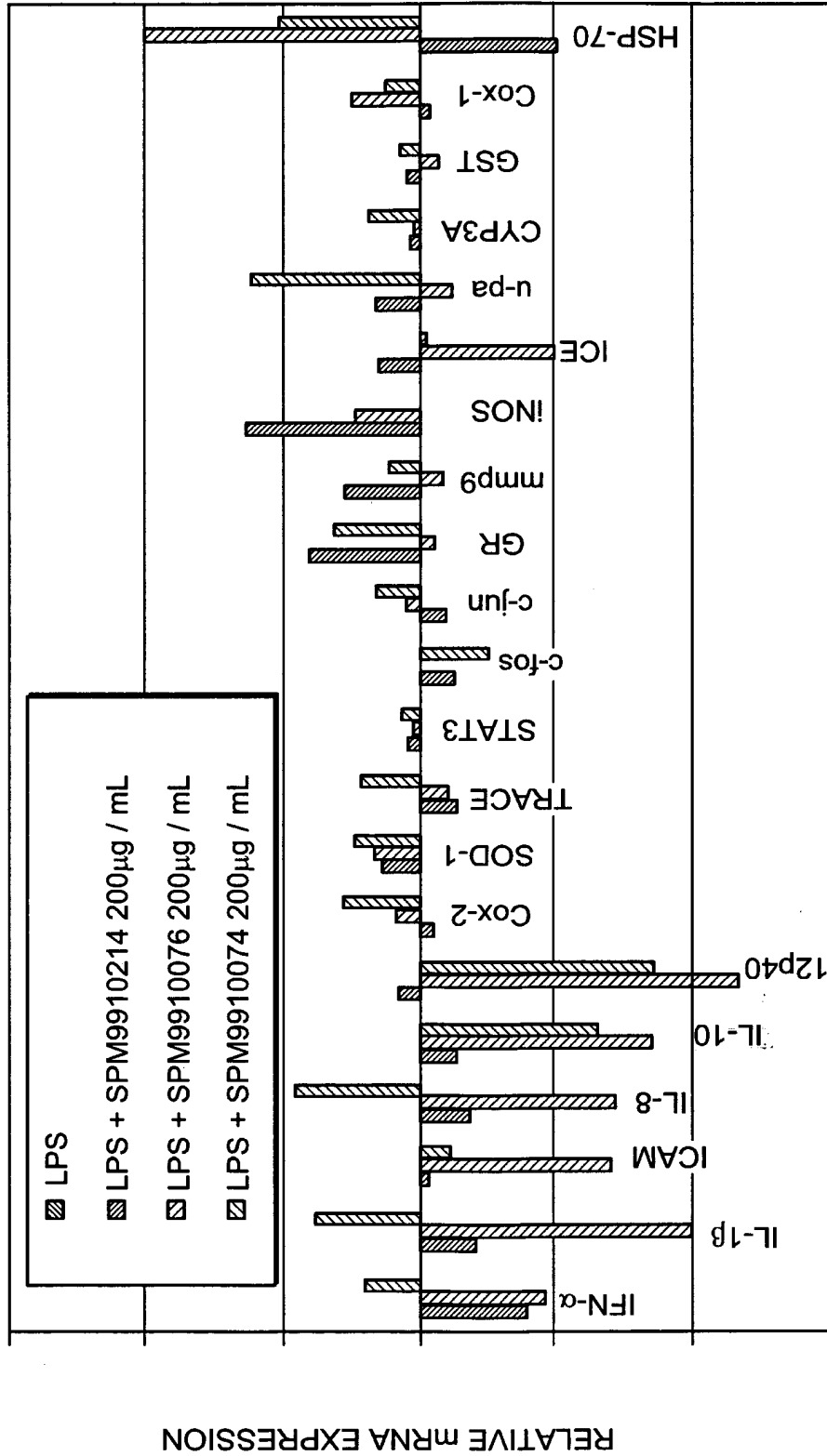
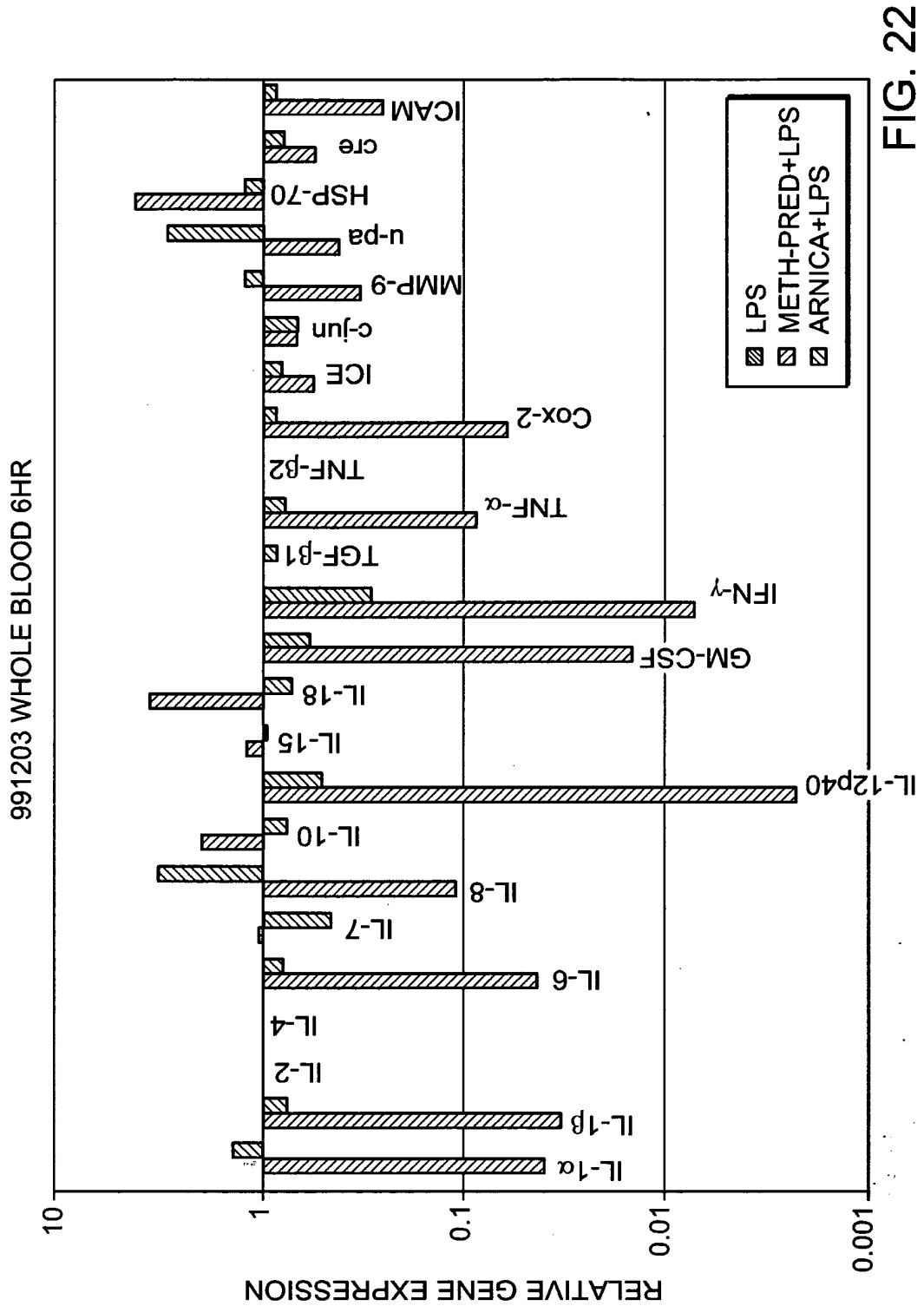


FIG. 21





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SELECTED PROFILES CAN CORRELATE WITH A DOSE RESPONSE FOR A GIVEN HERBAL

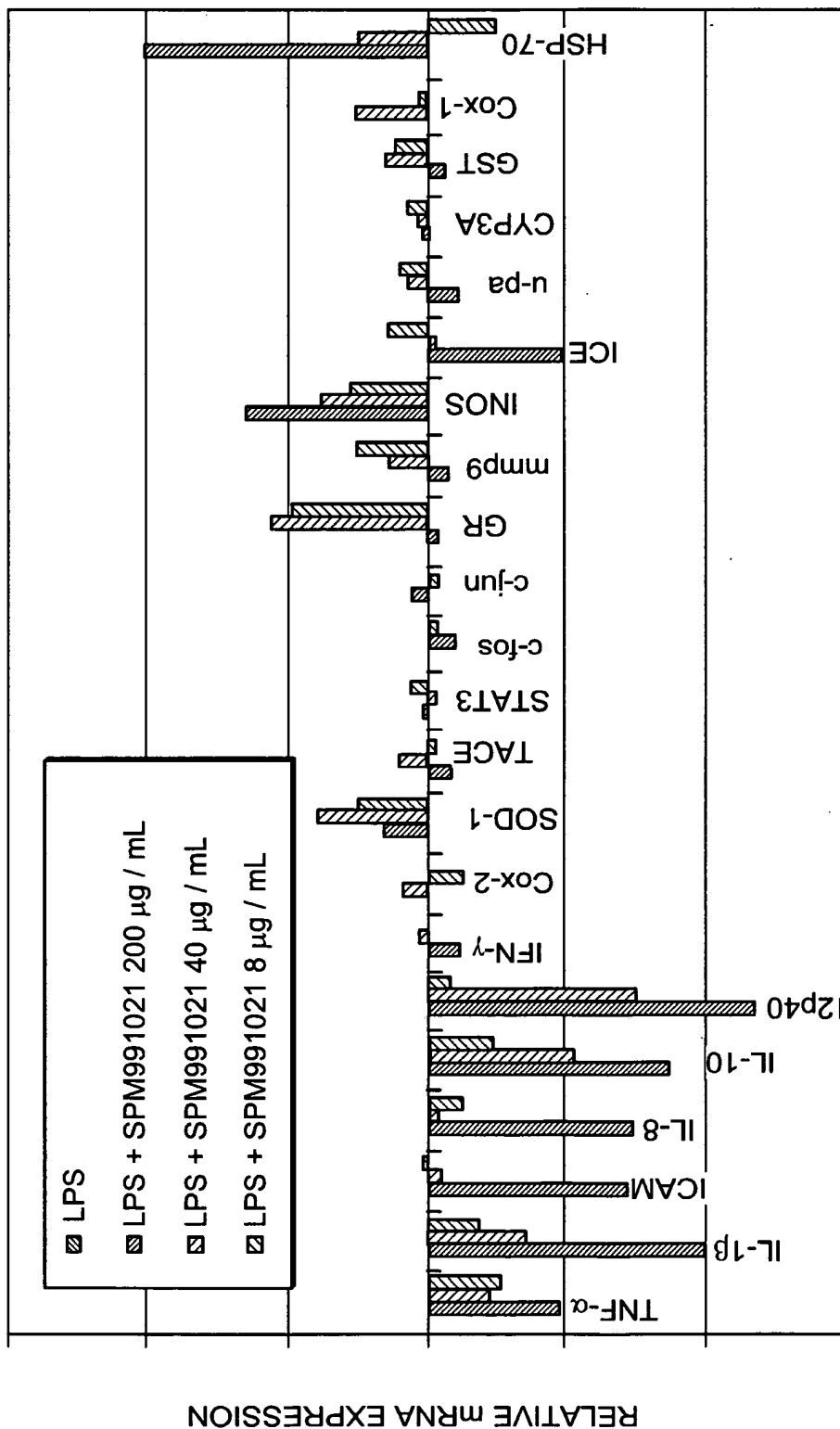


FIG. 23



SELECTED PROFILES REVEAL CONTAMINATION WITH ENDOTOXIN
AMONG DIFFERENT COMMERCIAL BRANDS AS REVEALED IN SPM010
AND SPM016

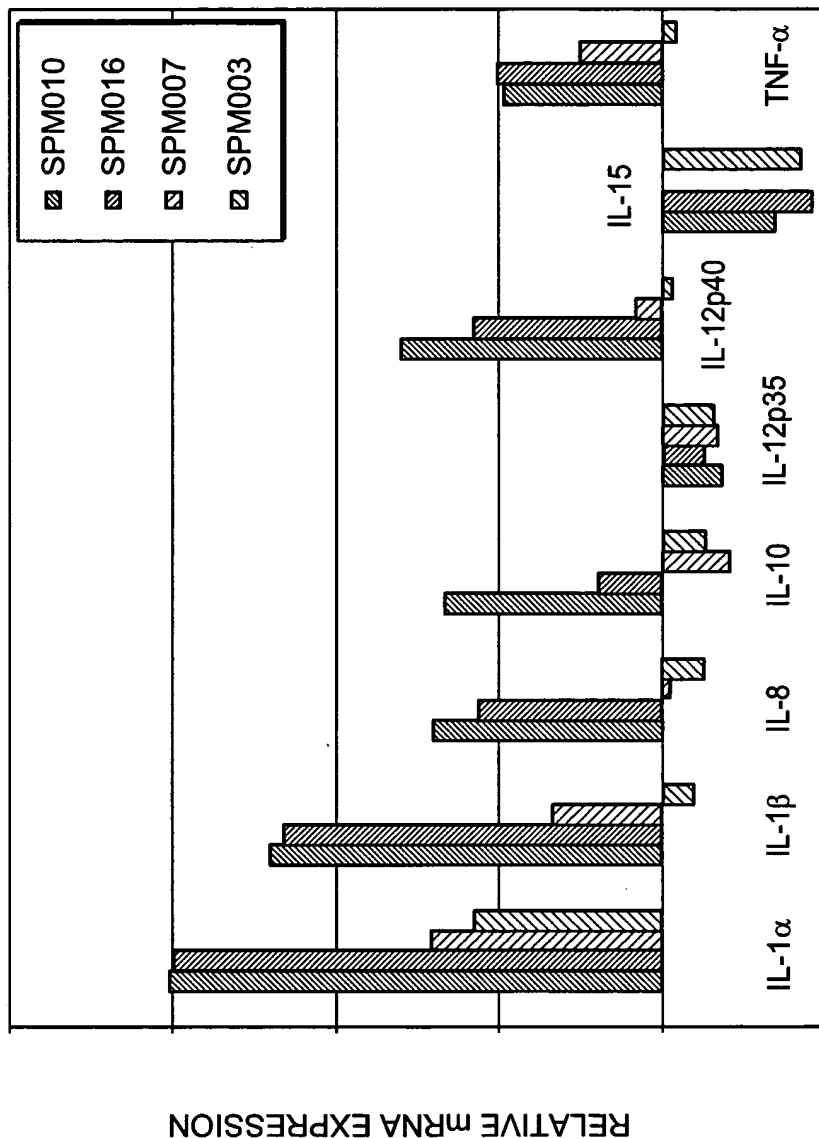


FIG. 24



HIGH DOSE COMPARISON OF UNSTIMULATED THP-1 CELL TREATMENT WITH THREE HERBAL PREPARATIONS SHOWS SIGNIFICANT VARIATION IN EFFICACY

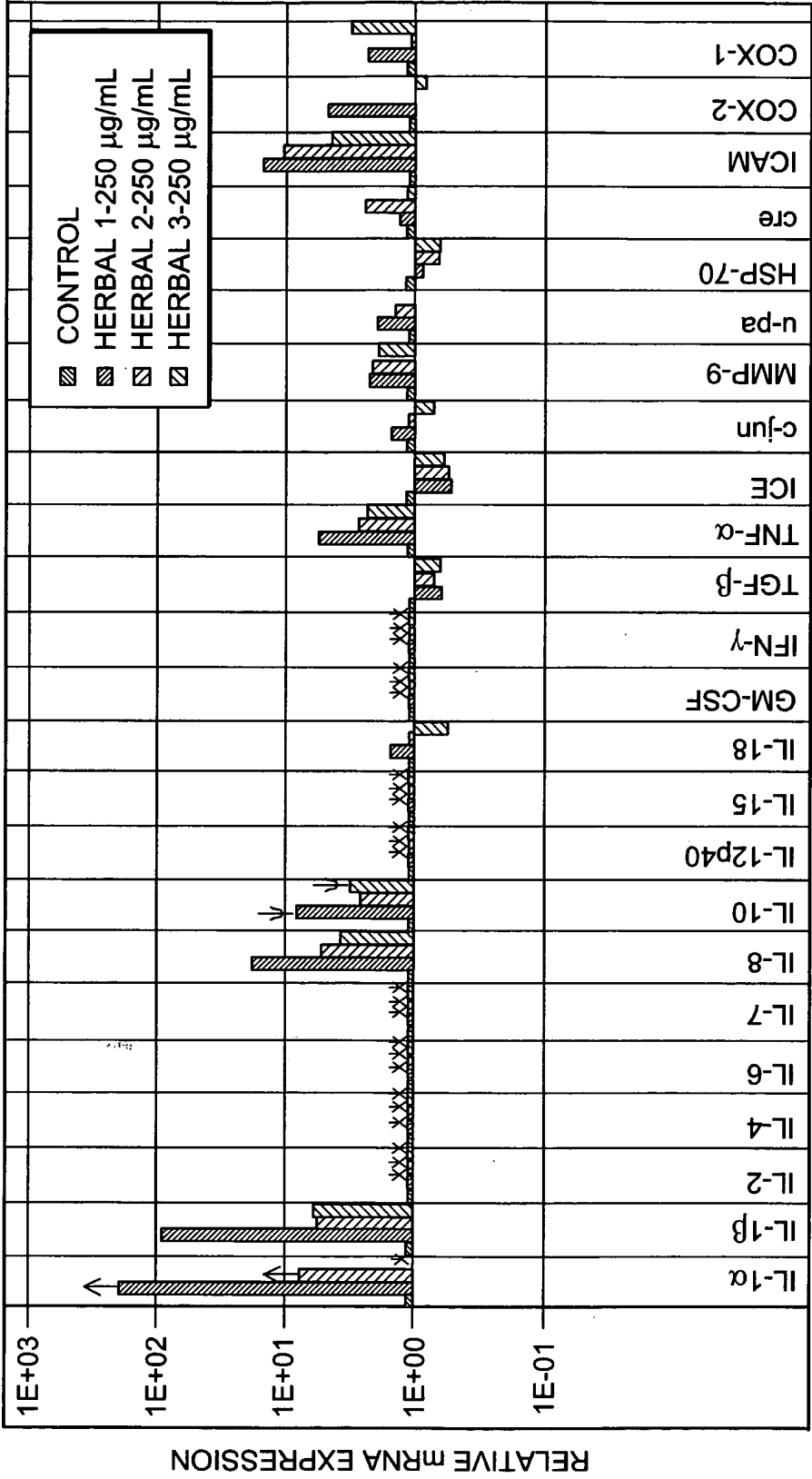


FIG. 25a



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TREATMENT OF UNSTIMULATED THP-1 CELLS WITH A SINGLE HERBAL SHOWS A NICE DOSE RESPONSE AMONG A SUBSET OF GENES

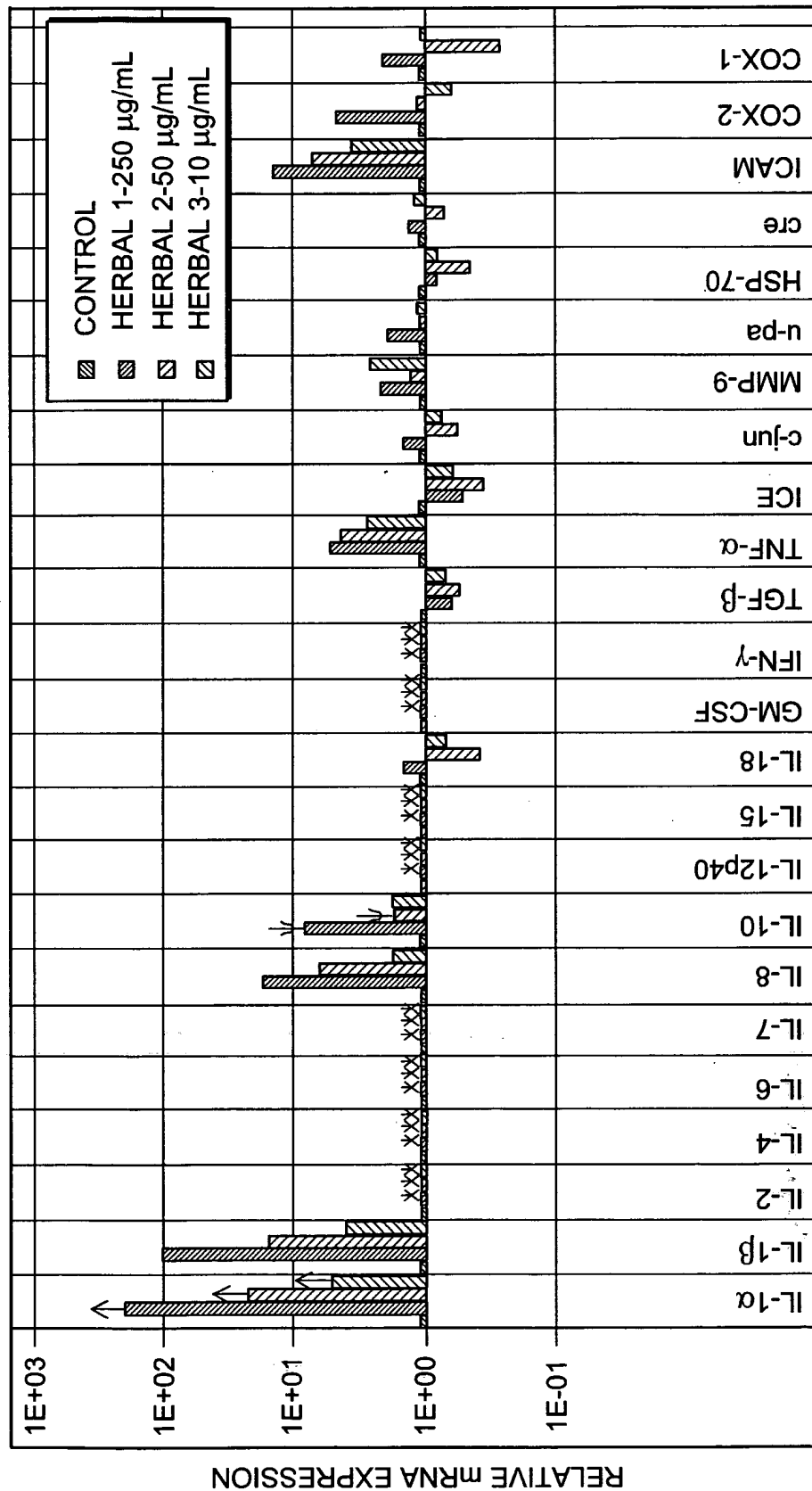


FIG. 25b



SELECTED PROFILES ALLOW FOR COMPARISON OF
COMMERCIAL ECHINACEAS (E1-E4)

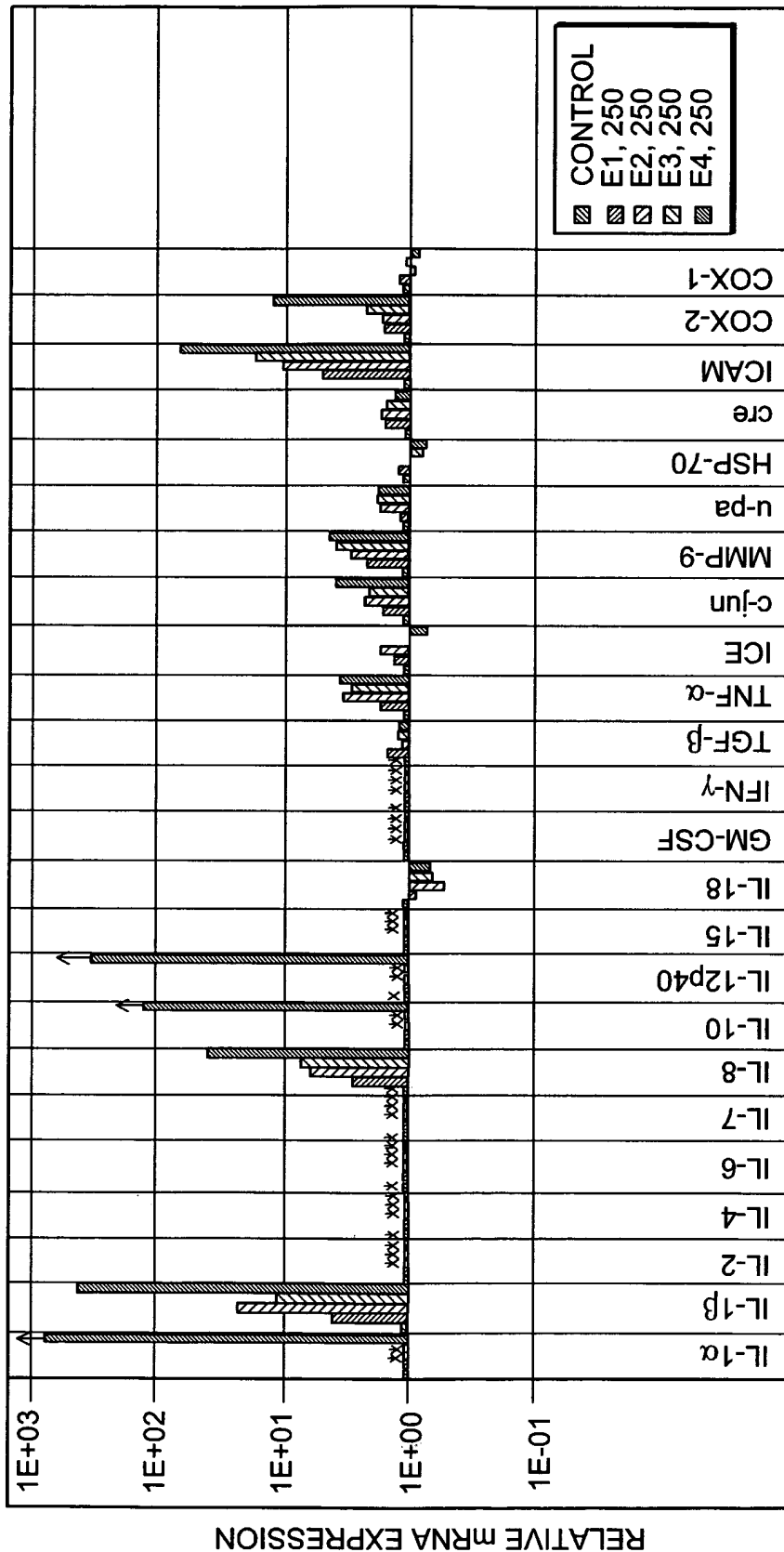


FIG. 25c



INFLAMMATION SELECTED PANEL SUBSET
DEMONSTRATES STEROID RESPONSE IN 3 DAY STUDY

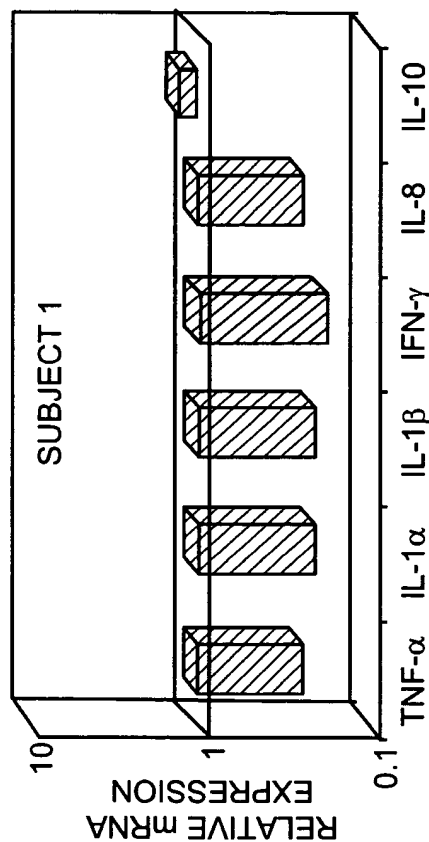


FIG. 26a

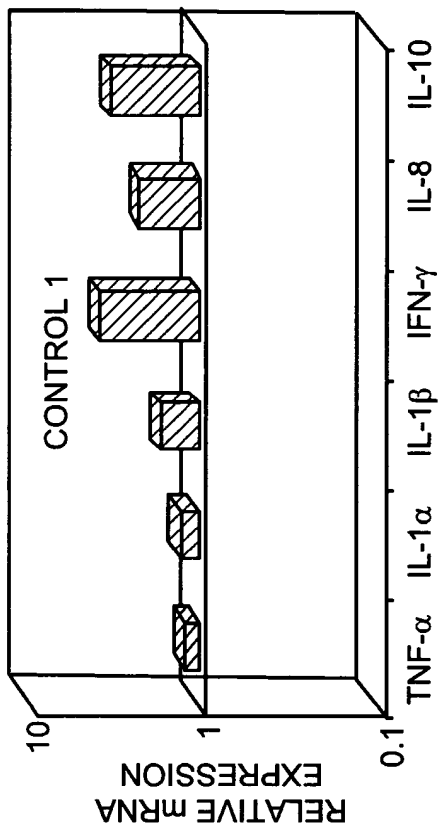


FIG. 26b

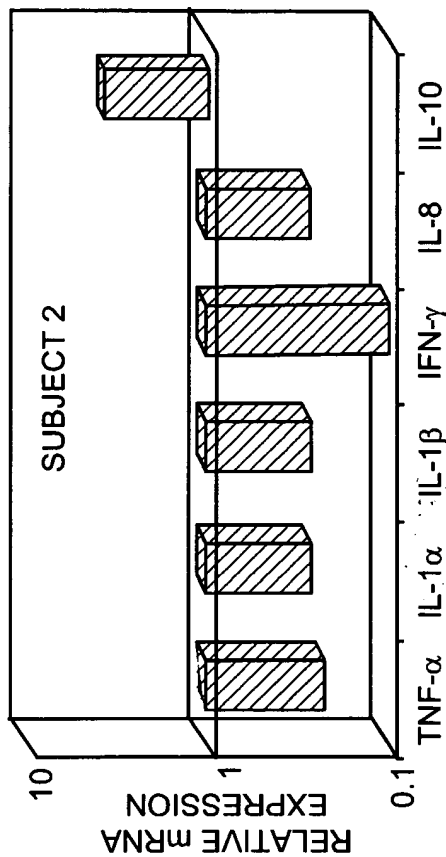


FIG. 26c

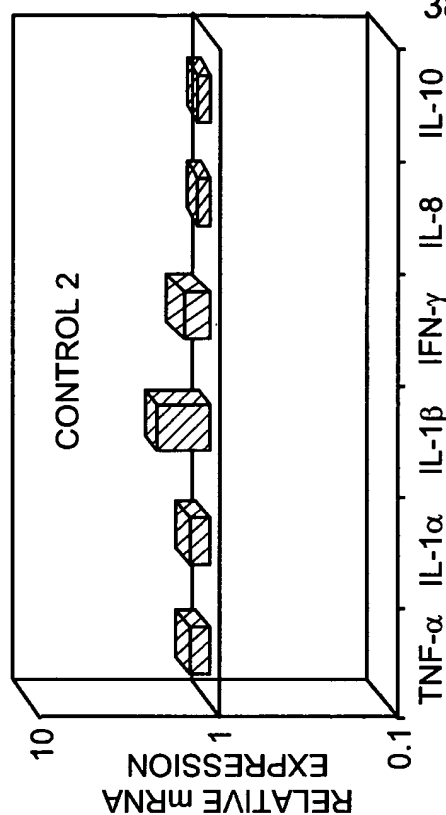


FIG. 26d



COMPARISON OF METHYLPREDNISONE AND HIGH-DOSE
IBUPROFEN IN PATIENTS USING INFLAMMATION SELECTED PANEL SUBSET

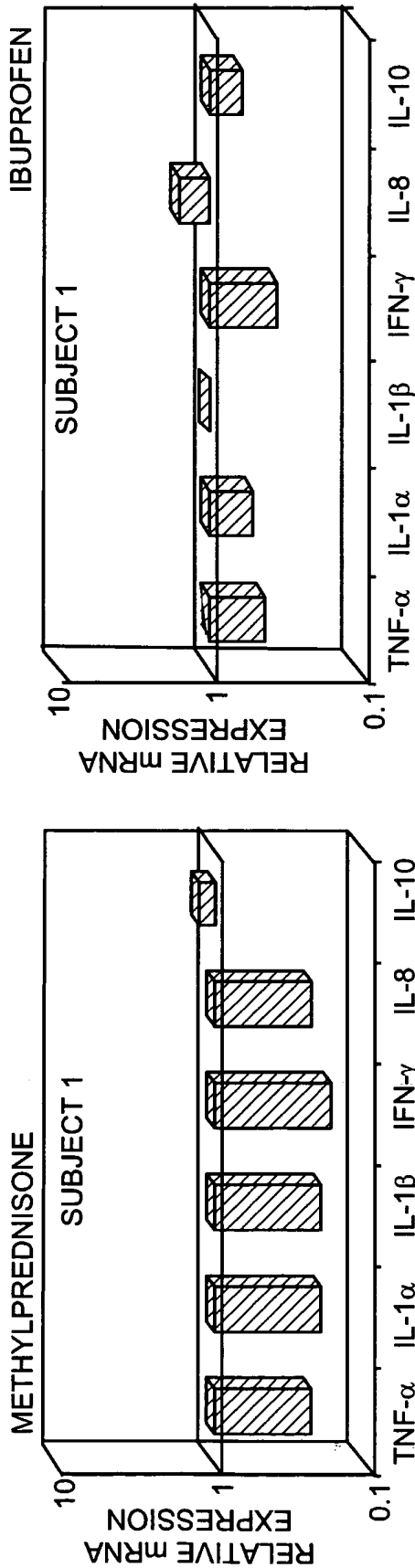


FIG. 27b
IBUPROFEN

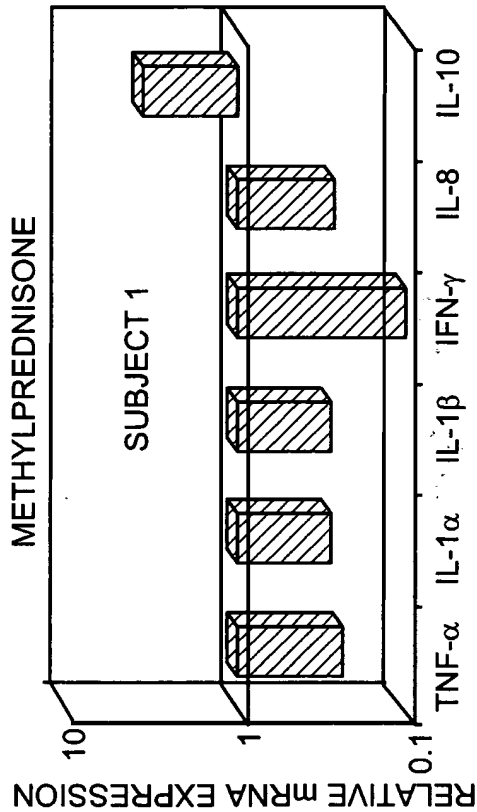
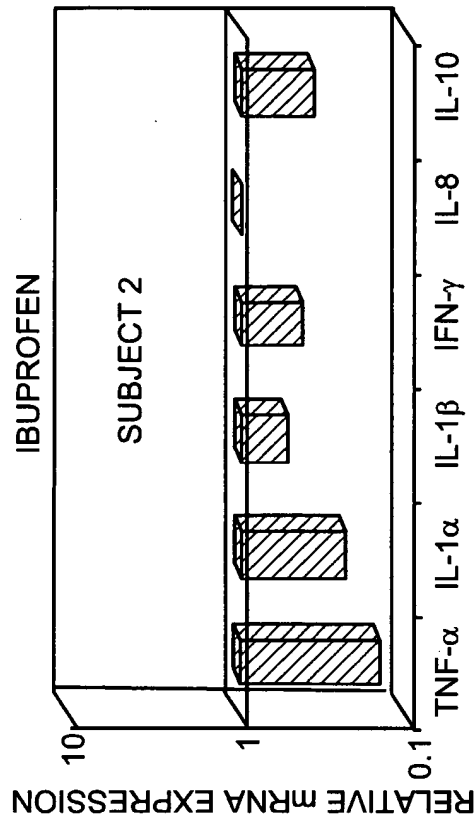


FIG. 27d

FIG. 27c



INFLAMMATION SELECTED PANEL SUBSET IDENTIFIES COPD PATIENTS

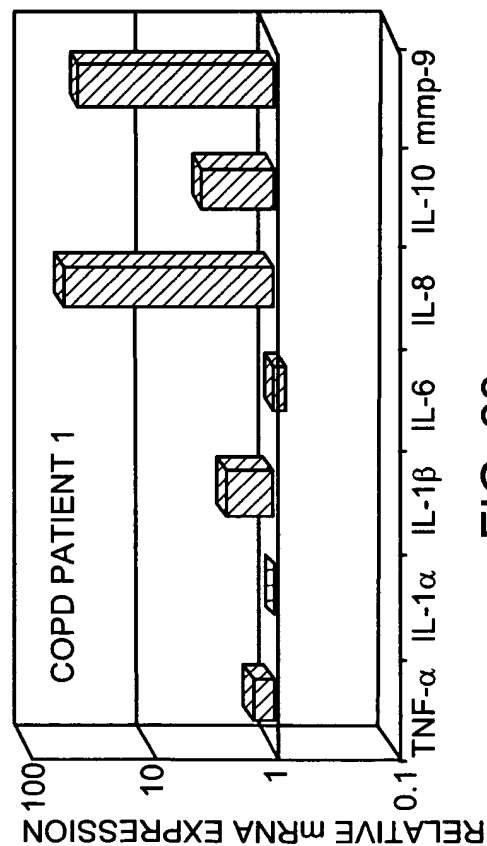


FIG. 28a

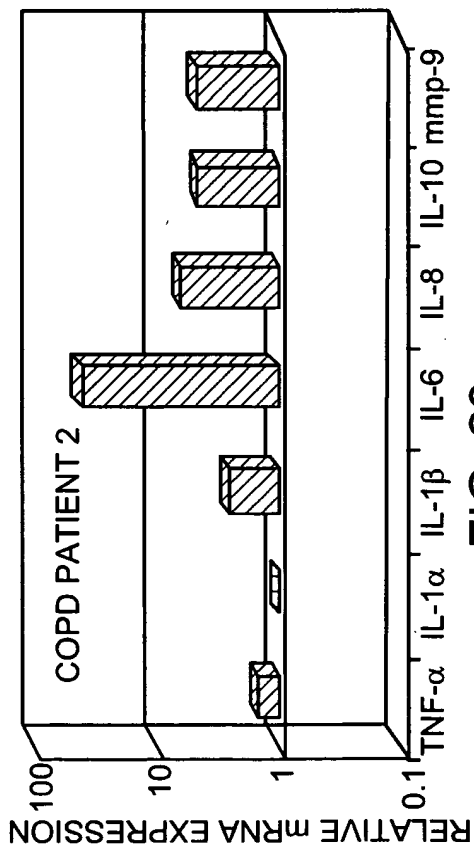


FIG. 28c

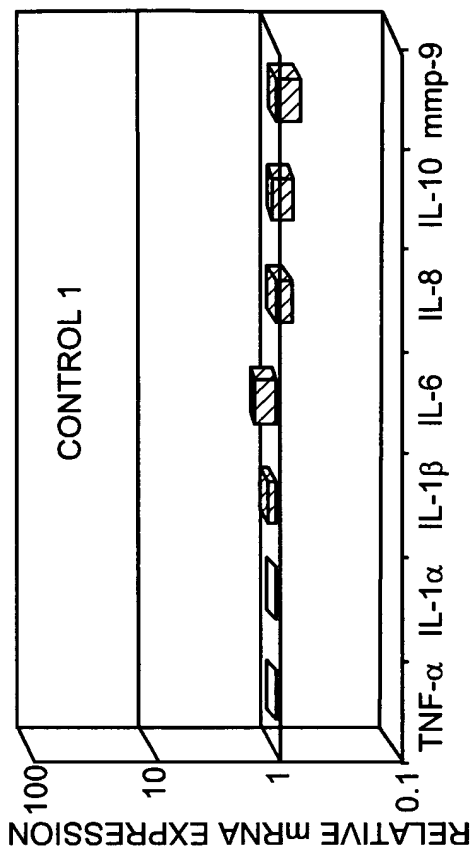


FIG. 28b

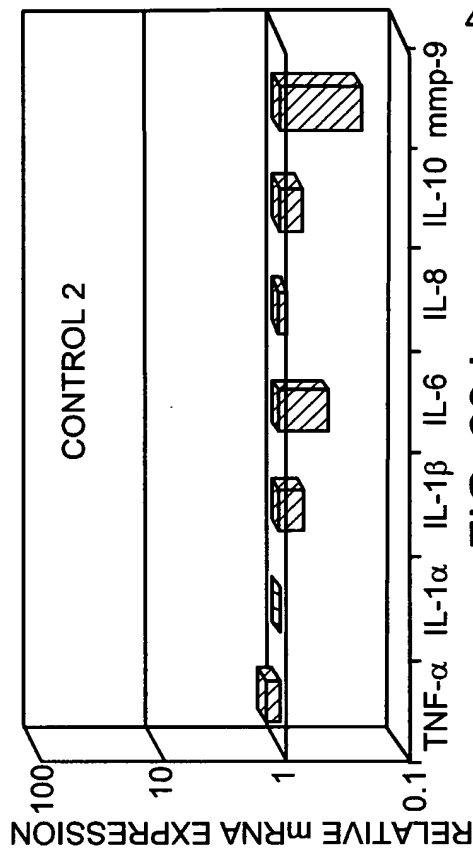


FIG. 28d



COMPARISON OF CALIBRATED PROFILE DATA SETS (USING INFLAMMATION SELECTED PANEL SUBSET) AFTER IN-VITRO AND IN-VIVO DRUG EXPOSURE (STEROIDS)--STUDY 1

AUGUST 1999
SUBJECT 1JC

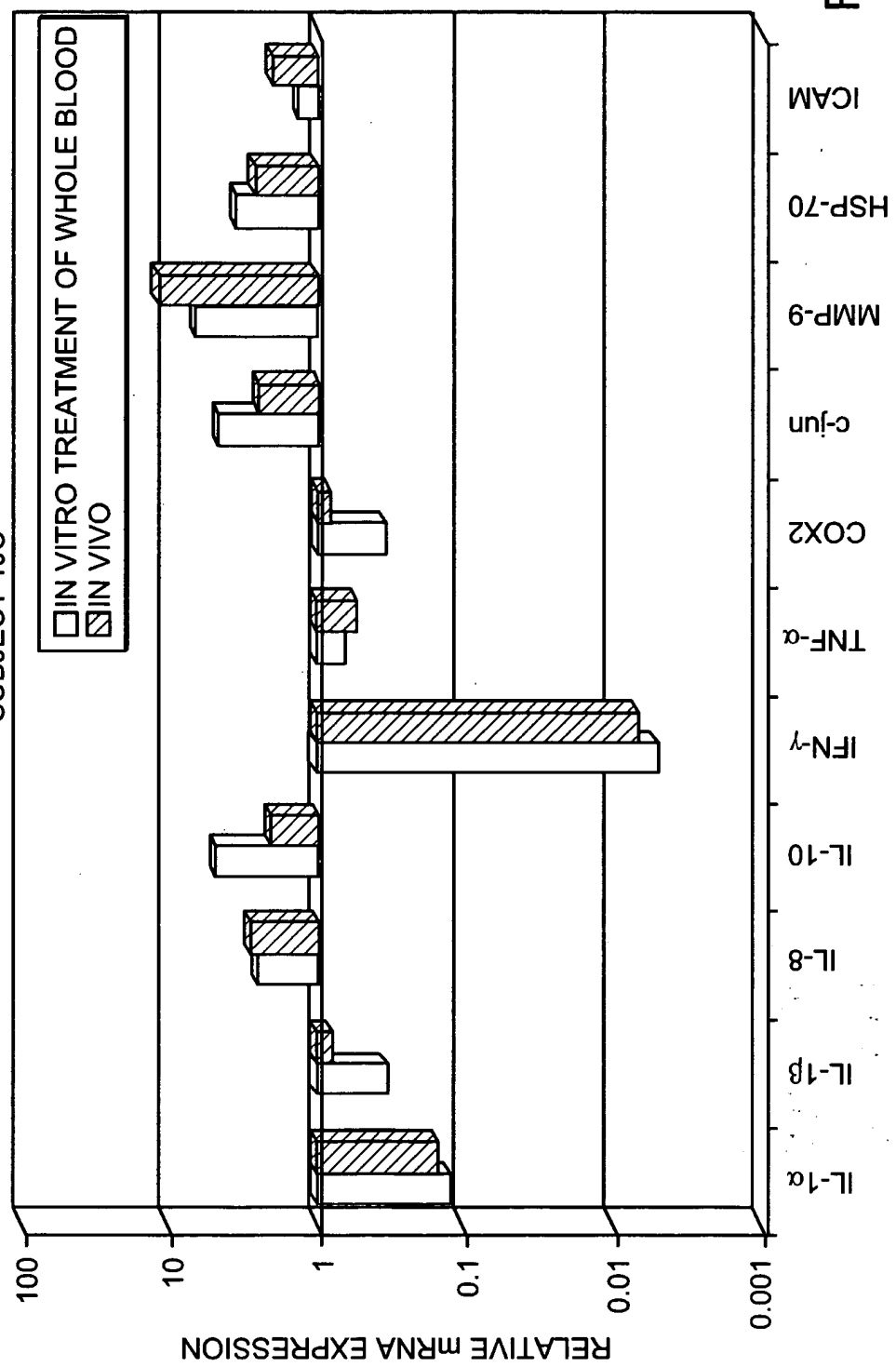
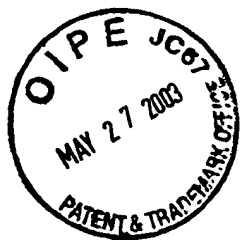


FIG. 29a



COMPARISON OF CALIBRATED PROFILE DATA SETS (USING INFLAMMATION SELECTED PANEL SUBSET) AFTER IN-VITRO AND IN-VIVO DRUG EXPOSURE (STEROIDS)--STUDY 2

AUGUST 2000
SUBJECT 1JC

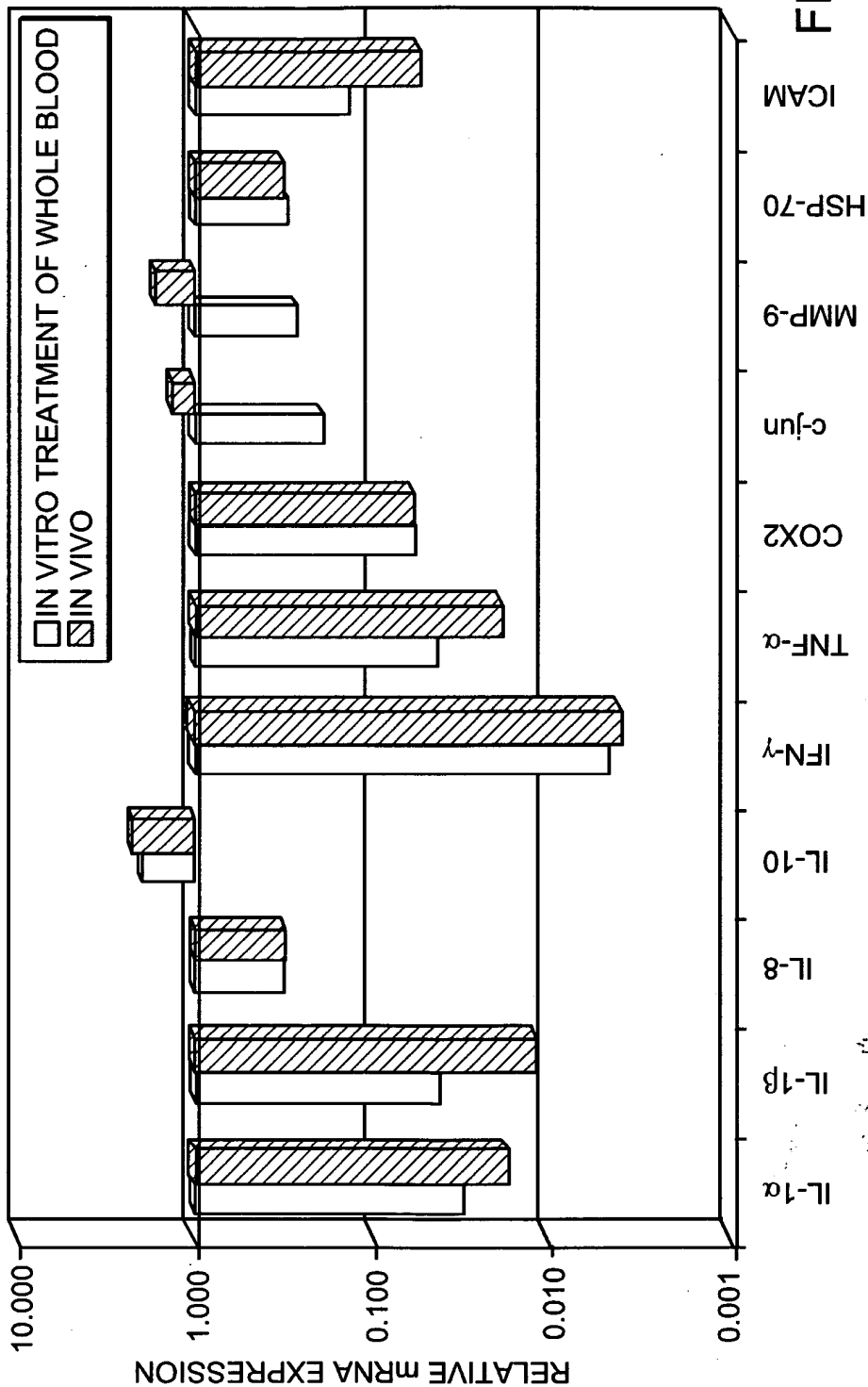


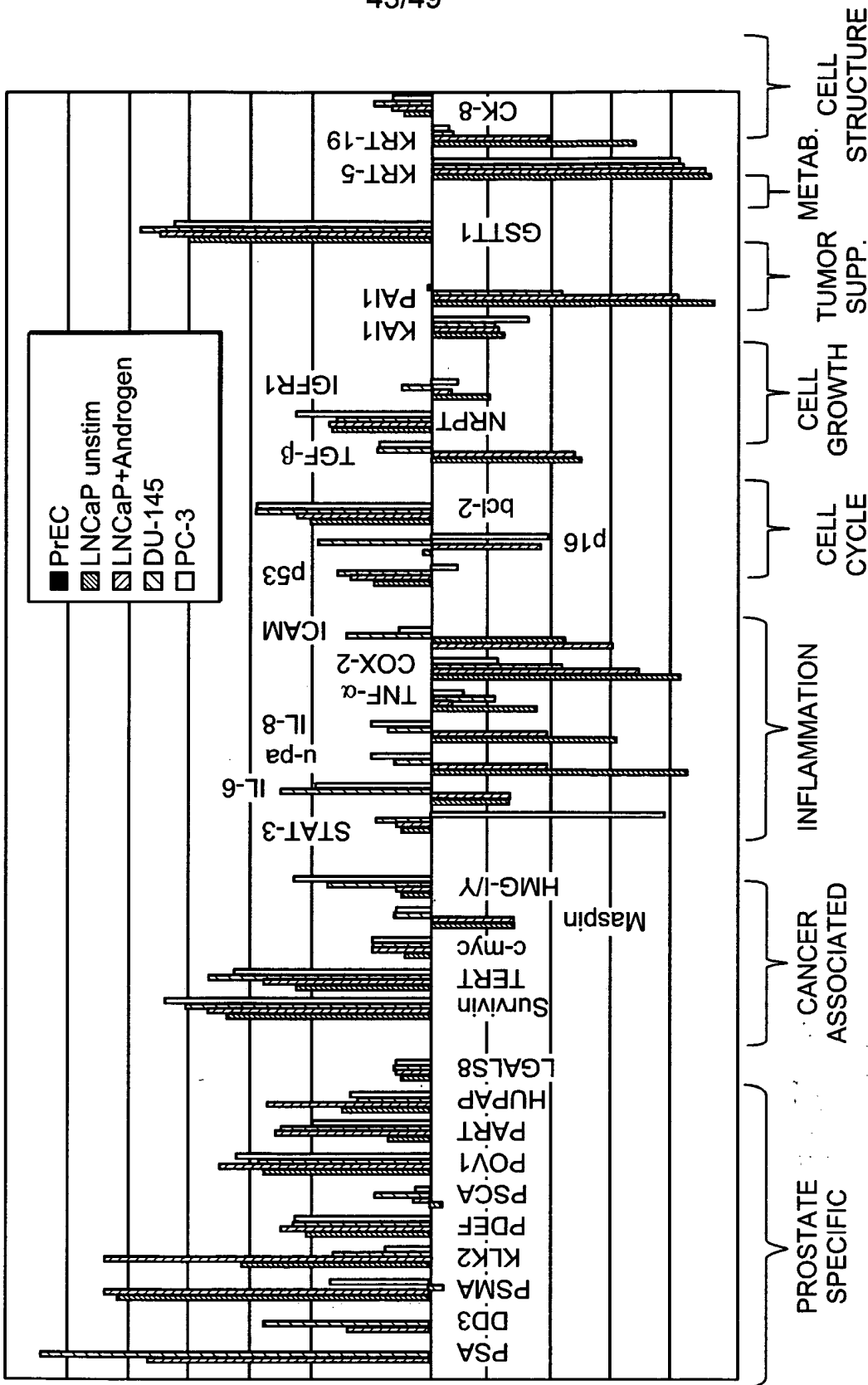
FIG. 29b



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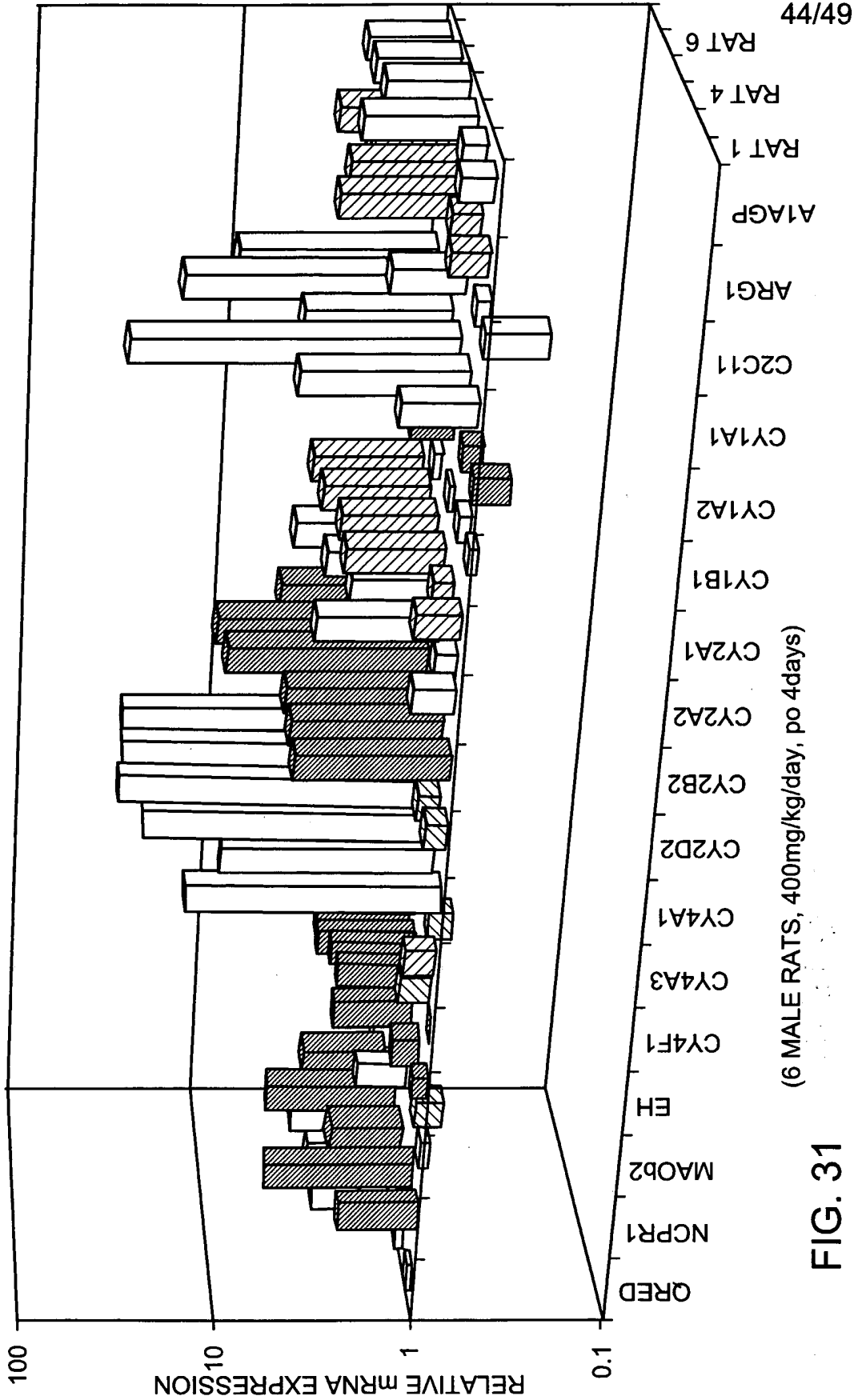
FIG. 30

EFFECT OF DIFFERENT AGENTS EVALUATED USING A SUBSET OF THE SELECTED PROSTATE PANEL, AND SHOWING BROAD FUNCTIONS OF PANEL CONSTITUENTS





EFFECT OF THE PHARMACEUTICAL CLOFIBRATE AS MEASURED ON RAT LIVER METABOLISM SELECTED PANEL





A METABOLISM SELECTED PANEL DIFFERENTIATES DRUG RESPONSES IN RATS.

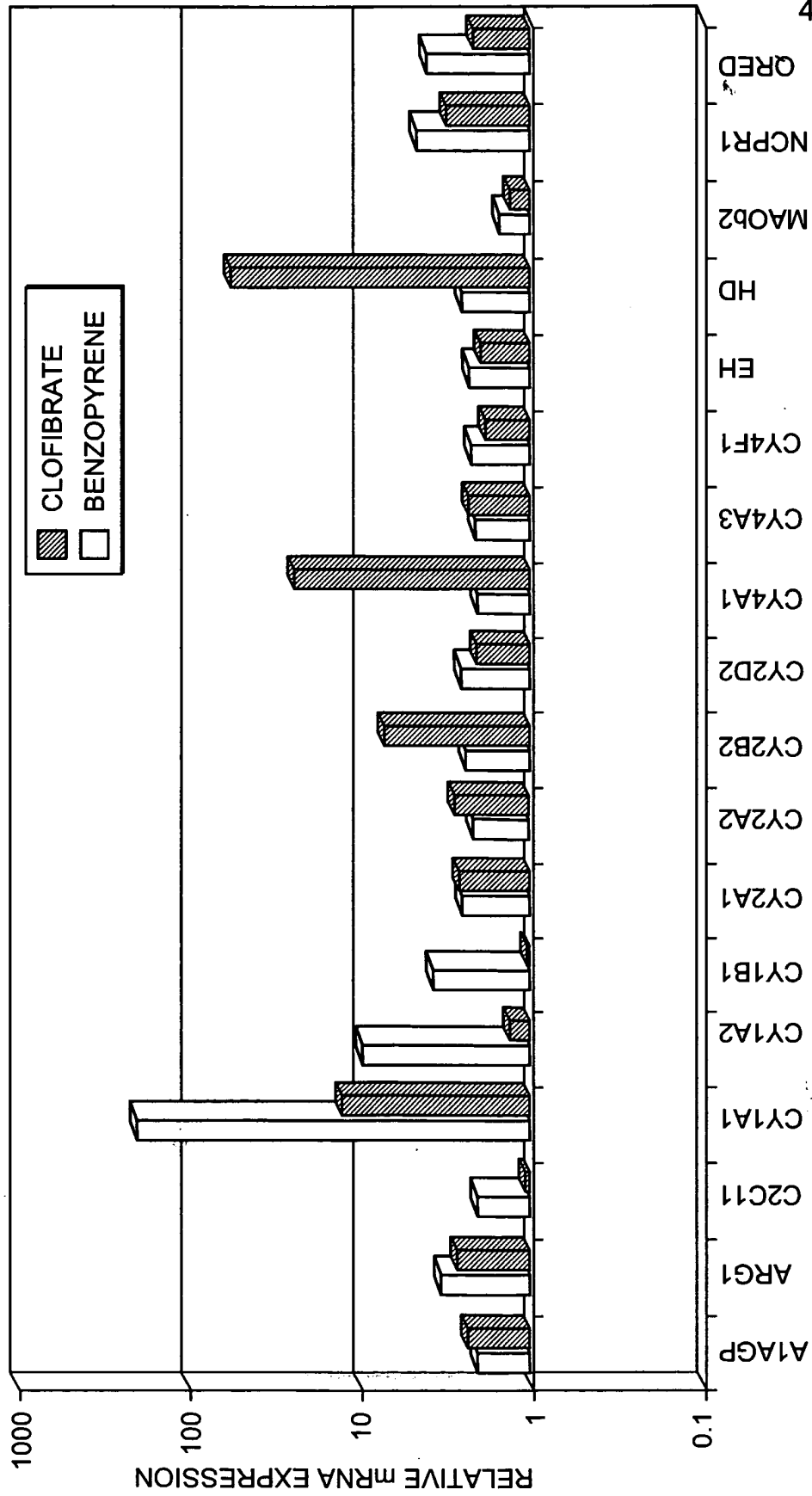
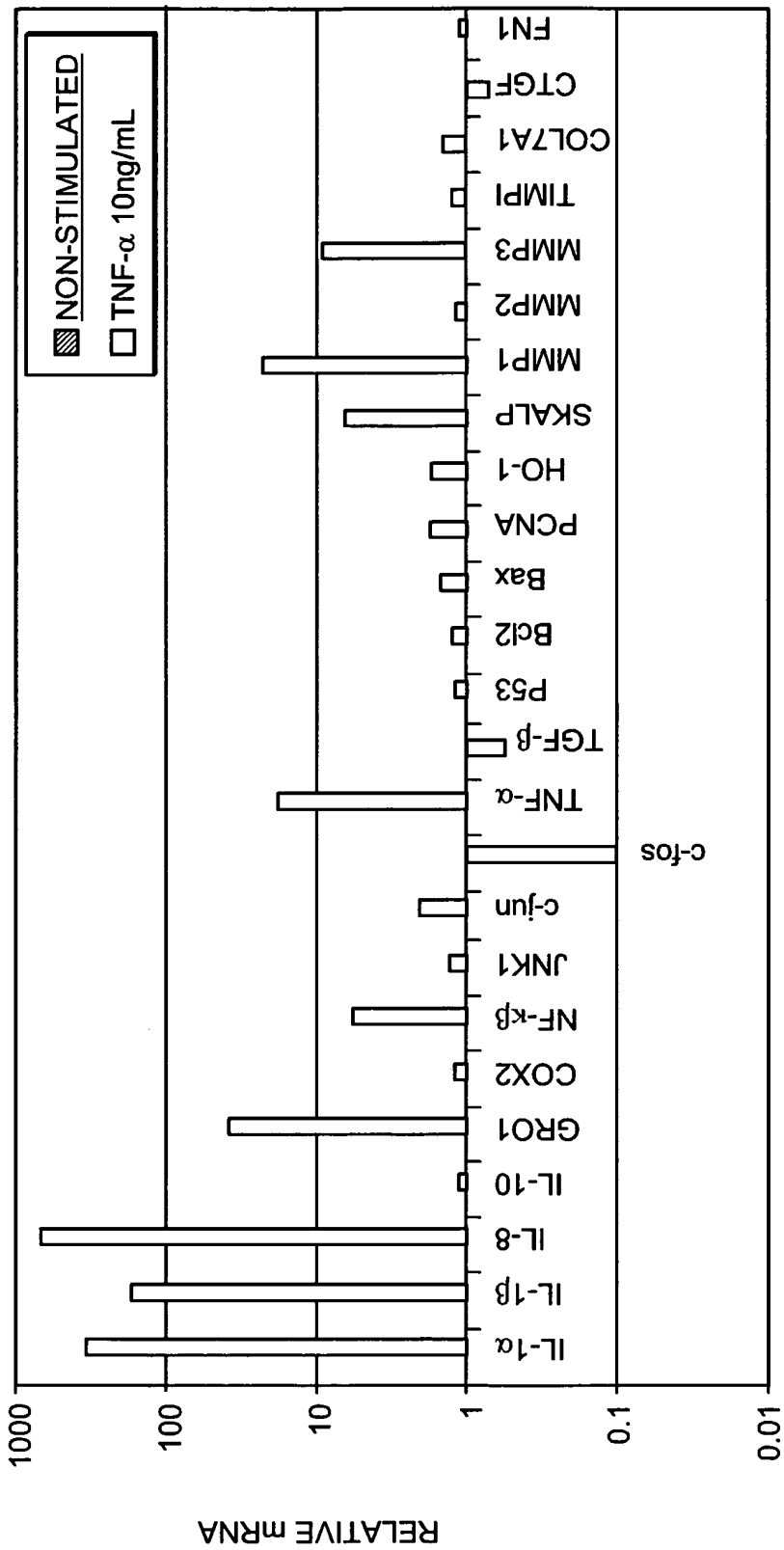


FIG. 32



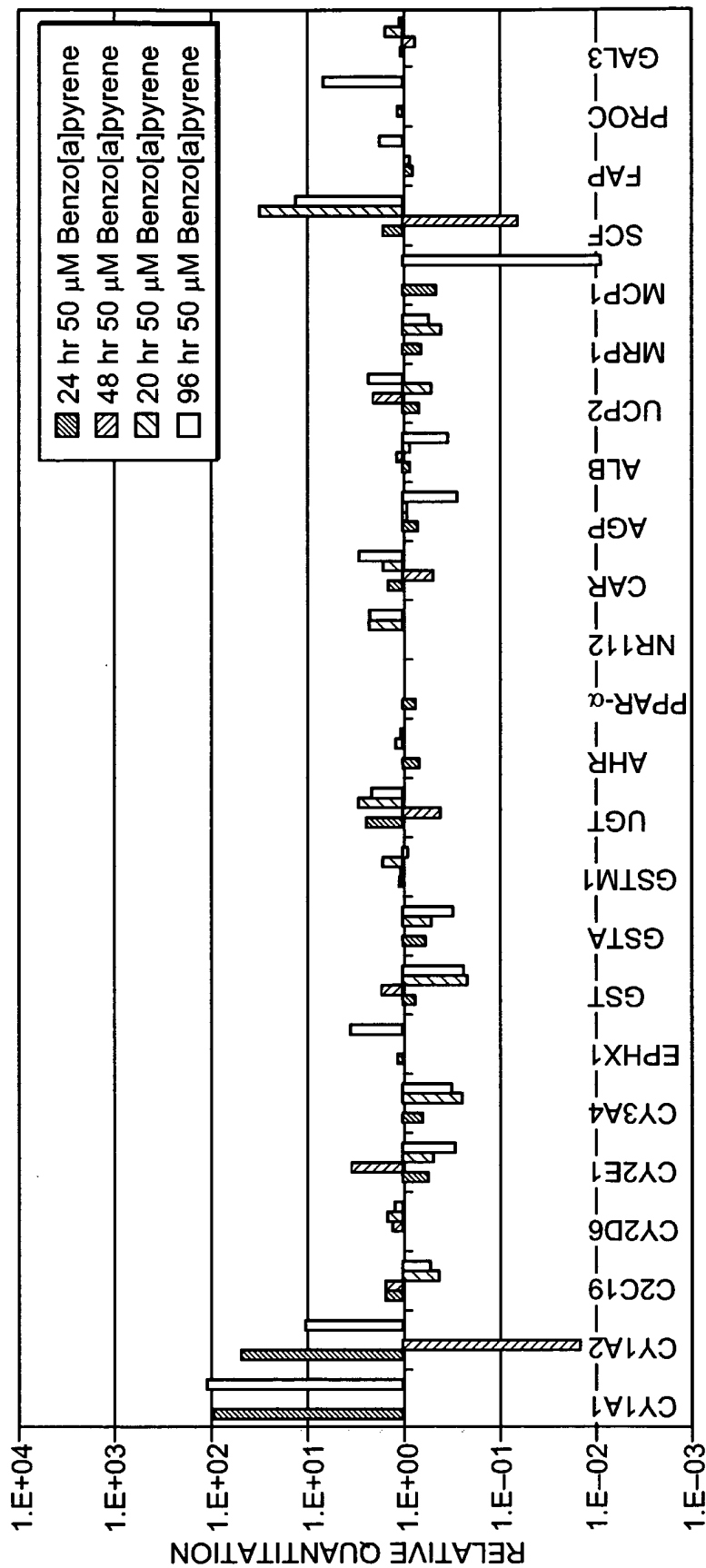
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A COMBINATION OF THE SKIN/EPITHELIAL AND VASCULAR SELECTED PANELS SHOW THE EFFECT OF ADMINISTRATION OF A STIMULANT.





EXAMPLE USE OF THE HUMAN LIVER SELECTED PANEL



Loci

FIG. 34



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HUMAN UMBILICAL VEIN CELLS TREATED WITH TNF- α AND ASSAYED ON THE VASCULAR SELECTED PANEL
HUVEC STIMULATED WITH TNF- α , t = 24hr

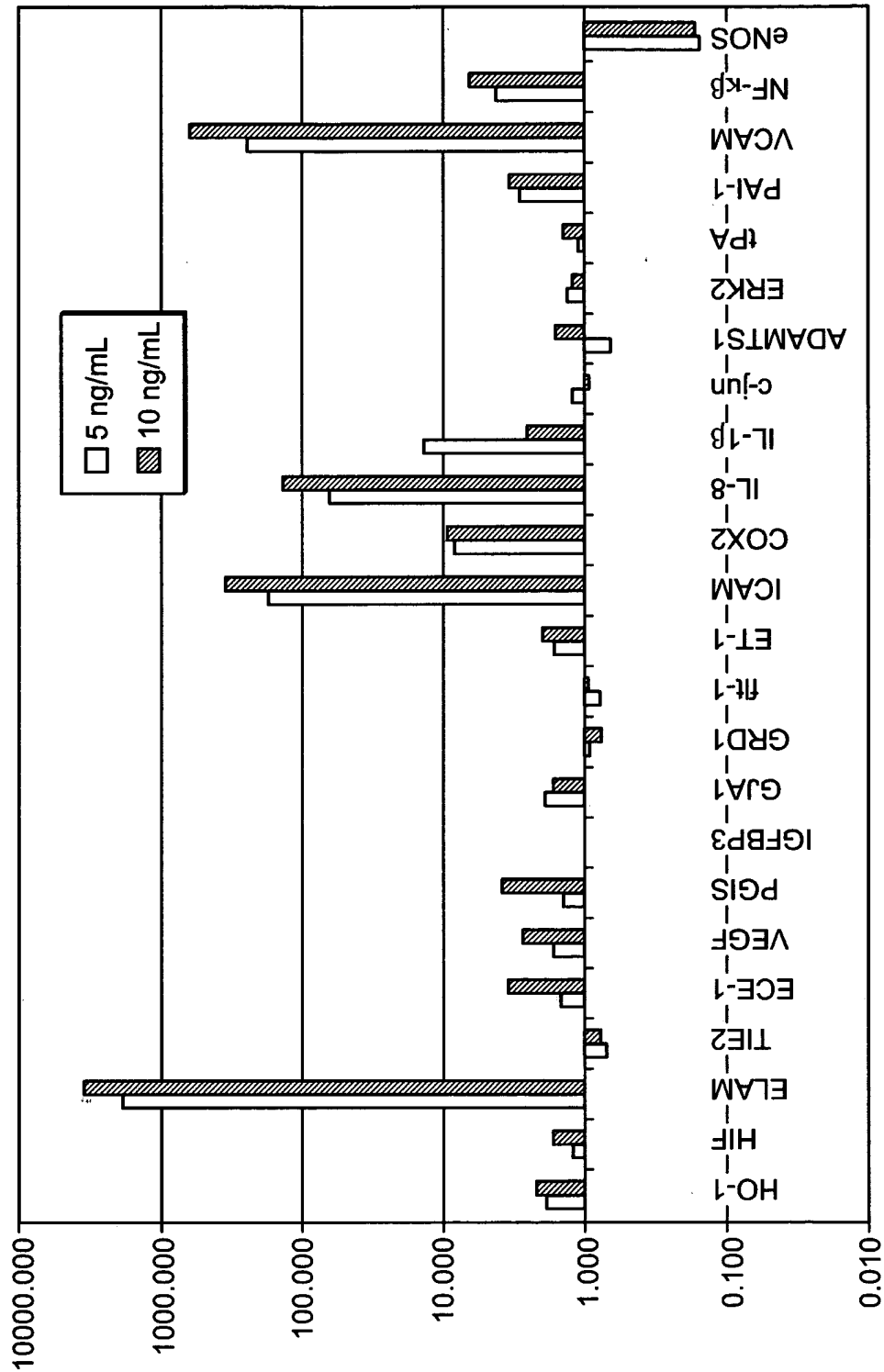


FIG. 35



ASSAY OF STIMULATED, HUMAN KERATINOCYTES ON THE SKIN SELECTED PANEL
EFFECTS OF N-ACETYLCYSTEINE ON UVB-STIMULATED KERATINOCYTES

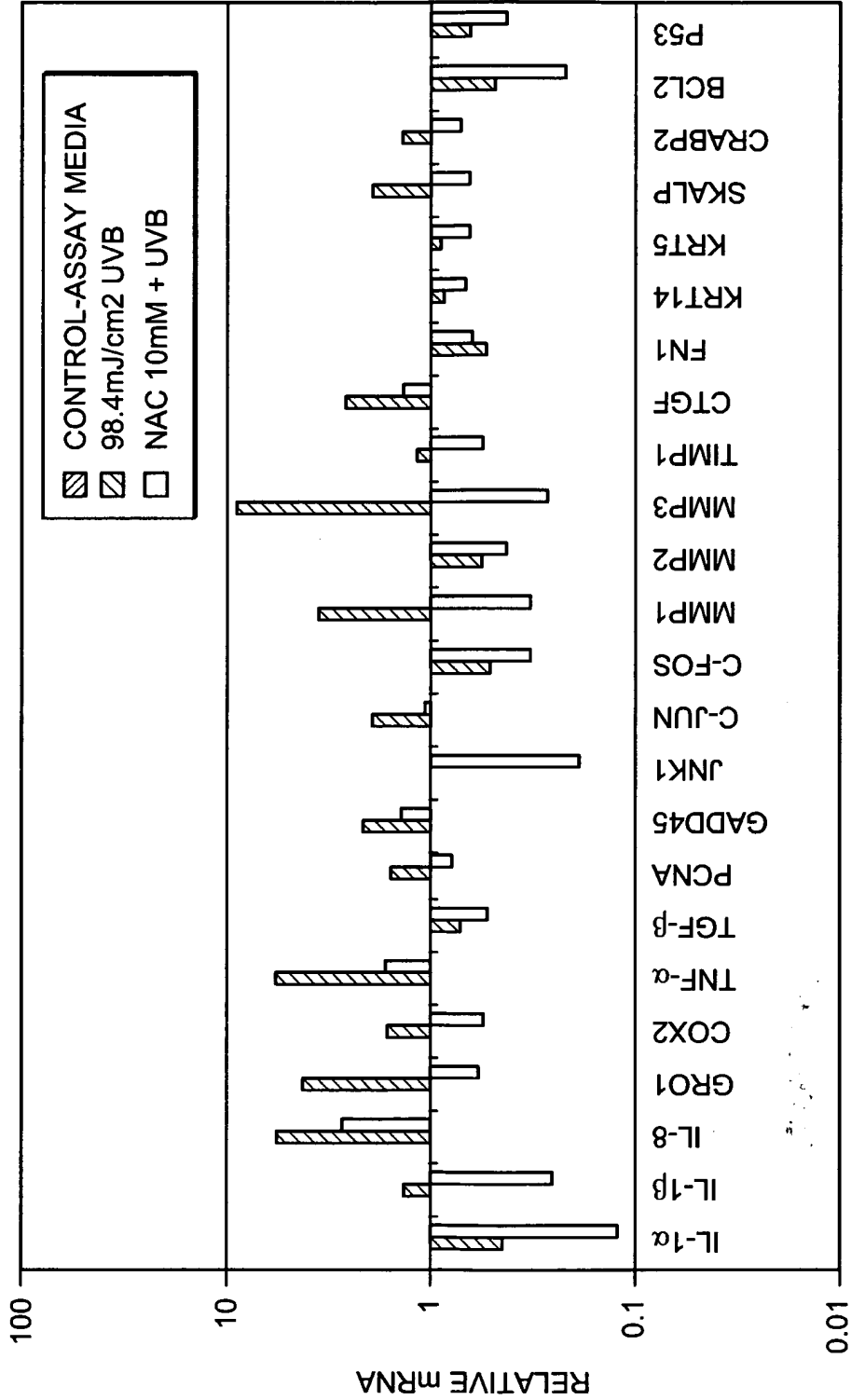


FIG. 36